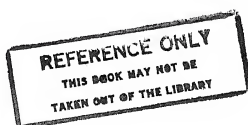


Categorisation of pathogens according to hazard and categories of containment



© *Crown* copyright 1984
First published 1984

Any enquiries regarding this publication
should be addressed to the Health and Safety
Executive at any area office or to the public
enquiry point, St Hugh's House, Trinity Road,
Bootle, Merseyside L20 3QY, tel. 051 951 4381.

ISBN 0 11 883761 3

Contents

Foreword	<i>iv</i>
-----------------	-----------

Preface	<i>v</i>
----------------	----------

Members of the Advisory Committee on Dangerous Pathogens	<i>vi</i>
ACDP working group	<i>vii</i>
Terms of reference of ACDP	<i>vii</i>

Introduction	<i>1</i>
---------------------	----------

Categories of pathogens	<i>4</i>
Definition of hazard groups	<i>4</i>
Allocation of pathogens to hazard groups	<i>4</i>
Bacteria, Chlamydia, Rickettsiae and Mycoplasmas	<i>5</i>
Fungi	<i>6</i>
Parasites	<i>7</i>
Viruses	<i>7</i>

Categories of containment	<i>9</i>
Model code of practice	<i>9</i>
Laboratory containment levels	<i>10</i>
Containment level 1	<i>10</i>
Containment level 2	<i>11</i>
Containment level 3	<i>12</i>
Containment level 4	<i>13</i>
Tabular summary of laboratory containment requirements	<i>15</i>
Animal room containment levels	<i>16</i>
Animal containment level 1	<i>17</i>
Animal containment level 2	<i>17</i>
Animal containment level 3	<i>18</i>
Animal containment level 4	<i>19</i>

Appendices	
A The use of class II microbiological safety cabinets	<i>22</i>
B Respiratory protective equipment	<i>23</i>
C Containment of latently infected animals	<i>24</i>
D Invertebrates	<i>27</i>
E Recommendations on physical containment requirements for work on specimens from patients who may be infected with Group 4 pathogens or rabies virus	<i>28</i>
F Containment facilities in high security isolation units	<i>35</i>
G Containment requirements for work with rabies virus materials	<i>36</i>
H Hepatitis B virus	<i>37</i>
I Training of laboratory personnel in microbiological safety	<i>43</i>
J Pathogens controlled by the Agriculture and Fisheries Departments	<i>44</i>

References	<i>48</i>
-------------------	-----------

Foreword by the Health and Safety Executive and the Health Departments

This report has been prepared by the Advisory Committee on Dangerous Pathogens (ACDP) and it contains the Committee's recommendations relating to work with micro-organisms. Although the guidance in the report does not have the force of either law or an approved code of practice under the Health and Safety at Work etc Act 1974, the Health and Safety Executive has instructed its inspectors to take it into account when considering whether there is compliance with statutory requirements.

Guidance on work with certain pathogens was published by the Department of Health and Social Security and other Government departments in 1976 in the handbook *Control of Laboratory Use of Pathogens Very Dangerous to Humans*. The guidance in the handbook has been overtaken by a number of recent developments, e.g. the Dangerous Pathogens Advisory Group has been replaced by ACDP and the Health and Safety (Dangerous Pathogens) Regulations 1981 have come into force. This report by ACDP is a further such development, and the 1976 handbook is now superseded.

Additional guidance on work with pathogens was published by the DHSS and other Government departments in 1978 in *The Code of Practice for the Prevention of Infection in Clinical Laboratories and Post-Mortem Rooms* (commonly known as the Howie Code). The guidance given in this report by ACDP on the hazard classification of pathogens, the levels of containment for work with pathogens, and the handling of specimens from patients who may be infected with Group 4 pathogens or rabies virus now supersedes the corresponding parts of the guidance in the Howie Code. The remainder of the Howie Code stands but is being reviewed by the Health Services Advisory Committee of the Health and Safety Commission.

The DHSS/Welsh Office booklet *Safety in Pathology Laboratories*, published in 1972, is no longer being issued because it is, in some respects, out of date. Those paragraphs relating to microbiological safety should be regarded as overtaken by the Howie Code and this report by ACDP.

Preface

The first task presented to the Advisory Committee on Dangerous Pathogens (ACDP) in June 1981 was to prepare a classification of pathogens according to hazard and to produce a code of practice for work with these pathogens.

We completed this work in January 1983 when a draft of our first report was submitted to Health and Agriculture Ministers and to the Health and Safety Commission (HSC). While we did of course draw extensively on published data in the scientific press, both in this country and abroad, our report was constructed with an increasing sense of the intrinsic problems of the subject and of our ignorance of many essential facts. It was mainly for these reasons that a recommendation was made by the Committee that the report should have wider consultation before receiving final endorsement. This recommendation was accepted and in March 1983 the report with a covering letter was sent to 42 bodies which have an interest in the field of microbiology. Following publicity on the release of the report some 340 individuals and organisations asked for and were given a copy of the report.

As a result of this widespread distribution, 110 written replies which contained comments and suggestions for revision were received and were carefully studied by the working group of the Committee. The draft was then amended to take account of these comments and this report, which has been agreed by the ACDP, can be taken as expressing the current consensus opinion of those who are engaged on work with pathogens. However, we recognise that it is not possible to write a final report on this subject: new pathogens will emerge or be discovered and new estimates of risk will be made as epidemiological and other data are collected and as new means of prevention and treatment emerge.

We would like to thank all those whom we have consulted who have given so freely of their time and expertise. Our thanks also go to those many individuals who either contributed to a collective response or replied in person when the earlier version of the Report was out for consultation. Their constructive criticism, advice, suggestions for amendment and encouragement were of great value to the Committee.

Advisory Committee on Dangerous Pathogens
December 1983

Members of the Advisory Committee on Dangerous Pathogens

The Secretary of State for Social Services, in his statement on the report of the investigation into the cause of the 1978 Birmingham smallpox occurrence, announced that the then existing control procedures for the laboratory use of dangerous pathogens were to be reviewed. Arising from that review, a new body called the Advisory Committee on Dangerous Pathogens was formed in May 1981 to replace the Dangerous Pathogens Advisory Group (DPAG).

The Committee consists of a chairman and ten specialist members together with five members representing employers and five representing employees. Appointments to the Committee are made jointly by Ministers and the Health and Safety Commission.

Chairman

Dr D A J Tyrrell, CBE, MD, FRCP, FRCPath, FRS

Specialist members

Mr F J Baker, OBE, FIMLS

Mr A J Barrow, FIMLS

Dr J H Connolly MD, FRCPI, FRCPath (from March 1983)

Dr R T D Emond, MB, ChB, FRCP, DTMH

Dr R J Fallon, BSc, MD, FRCP, FRCPath

Professor K B Fraser, MC, DSc, MD (until August 1982)

Dr A J Rowland, MB, ChB, DOBstRCOG, DPH, FFCM

Professor D I H Simpson, MD, FRCPath, FIBiol

Dr C E Wilde, BSc, PhD, FRSC, MRCPPath

Professor P Wildy, MA, MB, BCh, FRCPath, FRSE

Dr H Williams Smith, PhD, DSc, FRCVS, FRCPath, DipBact, FRS

Employer representatives

Dr P W Muggleton, BSc, PhD

Professor J A Scott, MA, MD, FFCM

Dr R F Sellers, MA, ScD, PhD, MRCVS

Dr J E M Whitehead, MA, MB, FRCPath, DipBact

Professor H I Winner, MD, FRCP, FRCPath

Employee representatives

Miss C M Bannister, SRN, OHNC (from June 1983)

Mr M Bryant*, FIMLS

Mrs L Clark, RGN, RSCN, NNEB (until June 1982)

Dr R R Davies*, PhD, DSc

Ms S McKechnie*, MA

Dr R Owen*, MB, ChB, FFOM, DMJ, DIH, LRSC

* Nominated by the TUC

Departmental observers

Dr R H Raynes DHSS

Dr D M Walford DHSS

Mr D Neill DHSS, Northern Ireland

Mr R A David HSE

Dr D O Haines HSE

Mr W E O Jones HSE

Dr R Nourish HSE

Mr M S Chapman MAFF (until February 1983)

Mr A J Crowley MAFF

Mr D Sweasey MAFF (from April 1983)

Dr M C Williams MoD

Dr A D M McIntyre SHHD

Dr W C D Lovett Welsh Office (until May 1983)

Dr S Palmer Welsh Office (from May 1983)

Secretariat

Mr E J Morris	HSE (until February 1983)
Mr M S Chapman	HSE (from February 1983)
Dr D L H Robinson	DHSS (until January 1983)
Mr P Lister	DHSS (from January 1983)
Mr B D Squires	HSE

ACDP working group

A working group was set up at the first meeting of ACDP to undertake the preliminary detailed work on the classification of pathogens, the model code of practice, and subsequently the revision of the draft report following consultation.

Working group members

Professor P Wildy (Chairman)
Mr F J Baker
Mr M S Chapman (until February 1983)
Mr A J Crowley
Dr R R Davies
Dr R J Fallon
Ms S McKechnie
Dr R Nourish
Dr R Owen
Dr R F Sellers
Professor D I H Simpson
Dr D A J Tyrrell
Dr J E M Whitehead

Secretariat

Mr E J Morris (until February 1983)
Mr M S Chapman (from February 1983)
Dr D L H Robinson (until January 1983)
Mr P Lister (from January 1983)
Mr N Higham HSE (until April 1982)
Mr M Bailey HSE (from May 1982)

Terms of reference of ACDP

In accordance with priorities determined by Health and Agriculture Ministers and the Health and Safety Commission:

- (a) *to advise the Health Ministers;*
 - (i) What work in connection with dangerous pathogens is necessary for the furtherance of public health and what work should not be undertaken because it puts public health at risk;
 - (ii) on the scale of the facilities needed nationally to deal with necessary work of this character; and
 - (iii) on the appropriate conditions on which clearance should be given from the public health aspect (as distinct from the health and safety at work aspect) for the conduct of particular pieces of research or categories of diagnostic work with category A pathogens;
- (b) *to advise the Agriculture Ministers* on the corresponding issues in respect of pathogens which are dangerous to animals as well as to humans;
- (c) *to advise the Health and Safety Commission and the Health and Safety Executive on;*
 - (i) the general standards of safe working to be observed in work with dangerous pathogens in laboratories (but not advice on such standards in individual cases unless this is sought by the HSE);

- (ii) necessary improvements in facilities and working methods in general;
- (iii) new hazards from such pathogens; and
- (iv) the terms of any controls to be applied generally to laboratories working with such pathogens—regulations, codes of practice and guidance;
- (d) *to advise Health and Agriculture Ministers, the HSC and the HSE on:*
 - (i) the classification of pathogens according to the hazards they present;
 - (ii) the progress and significance of relevant medical and scientific research and developments; and
 - (iii) such other matters connected with work with dangerous pathogens as may be referred to the Committee by the HSC, the HSE or Ministers.

Introduction

1 Many reports published during the last 30 years have dealt with various aspects of microbiological safety. In this country interest was further stimulated by a series of events that began with an outbreak of smallpox in London in 1973 which originated from a laboratory acquired infection. This incident led to a succession of committees which were set up to provide guidance on the assessment of risks and to produce codes of practice for work with pathogens (The Cox Committee 1973¹, The Godber Working Party 1973², The Dangerous Pathogens Advisory Group 1975³, The Howie Working Party 1975⁴). Despite the guidance that these bodies provided, a further smallpox incident occurred in 1978 at Birmingham. An investigation into the incident (The Shooter Report 1978⁵) recommended that regulations should be made that require laboratories to notify their intention to hold or handle certain pathogens, and following this The Health and Safety (Dangerous Pathogens) Regulations 1981 came into force.

2 The Robens Report (1972)⁶ led to the establishment of the Health and Safety Commission (HSC) and the Health and Safety Executive (HSE) and to the Health and Safety at Work etc Act of 1974 (HSW Act). This Act provides a framework to encourage high standards of health and safety at work with all kinds of hazardous materials including micro-organisms. These latter agents may call for special attention, however, because of their inherent characteristics and because their effects on health may differ widely with variations in the susceptibilities of those individuals exposed. Nevertheless, the general principles of occupational hygiene that are adopted for work with all potentially hazardous materials, namely to minimise exposure of persons to the agent by primary and secondary containment of the work to a level appropriate to the nature of the risk, can be usefully applied for work with microbiological materials. We have constructed our report with these principles in mind.

Statement of intent

3 The philosophy and guidance offered in this report are aimed at the prevention of infection which might result from work with micro-organisms or materials which contain them. Our recommendations relate, in the main, to work where the identity of the organism is known and where there is an intention to manipulate or to propagate the organism itself. Thus, they are directed to all establishments where such microbiological work is carried out. There are however sections in this report which are of relevance also to laboratories specialising in disciplines other than microbiology. They may deal with specimens not intended for culture but which may nevertheless contain pathogens in sufficient concentration for a risk of infection to arise. We have not attempted to provide detailed guidance for work with clinical specimens except for those suspected to contain rabies virus or Group 4 pathogens. For work with clinical specimens reference should be made to the *Code of Practice for the Prevention of Infection in Clinical Laboratories and Post-mortem Rooms*⁴, which we recommend should be reviewed. The guidance on the various levels of containment, set out in the model code of practice (paras 22 to 43), are relevant also to those who have a responsibility for the design, building or alteration of premises where micro-organisms are handled.

Assessing the dangers of pathogenic organisms

4 The essential problem of assessment is simple: we require to know whether work with a particular organism causes death, disease or any inconvenience to those working with it and to know whether such work engenders any secondary dangers to the general population. The strategies for securing this knowledge are also straightforward. There are two and they are complementary. The first is epidemiological in which rates of infection and disease are analysed and the second is a synthesis of various attributes of organisms such as infectivity for man, stability in the environment, ability to infect by different routes and susceptibility to specific treatment and prophylaxis. Clearly it should be possible to produce balance sheets of all such properties and weigh them against the protection afforded by our recommended containment measures.

5 We devised several quantitative schemes to express in numerical terms the hazard and risks associated with individual organisms similar to those devised by the Genetic Manipulation Advisory Group. Although some of the schemes appeared workable for some organisms they have not been included in this report because they could not be applied generally owing to the lack of sufficiently reliable data and because they could not be properly evaluated.

6 We have therefore resorted to assessing each pathogen listed by getting a consensus of experts. We have taken account of the opinions of other bodies (e.g. the US Department of Health, WHO, DPAG, etc); summarised what is known of the severity and type of disease produced, including risks of oncogenicity, the route of infection, of stability in the environment, prevalence in the community, etc; and we have thoroughly discussed each pathogen that we list before assigning it to one of the four hazard groups (para 14). In certain particularly difficult examples, the scientific basis is briefly summarised in an Appendix (G and H).

Physical containment of work

7 We describe in the model code of practice four levels of physical containment for laboratories and animal rooms in which we think work with pathogens in the four hazard groups can be safely undertaken. We have dealt mainly with work where it is known which pathogens are being used and where the corresponding containment levels directly apply. In diagnostic laboratories, although there will be uncertainties about the presence of pathogens in the materials being investigated, the possibility that a pathogen classified in one of the higher hazard groups might be present, and the risk this presents, must be assessed. In order that appropriate containment measures may be taken, information as to the assessment must be made available by suitable means e.g. label or laboratory request form. Appendix E describes the containment levels appropriate for work with clinical specimens which are suspected of containing rabies virus or Group 4 pathogens. Where specimens for culture (other than those covered in Appendix E) are known or strongly suspected to contain a pathogen the guidance given in the model code of practice, as appropriate to the hazard group of the pathogen, should be followed. Where specimens for other tests are known or strongly suspected to contain a pathogen, an assessment must be made of the risk of infection based on both the nature of the work to be done and the hazard of the organism; more detailed and specific guidance and instruction will be found in national, industry and local codes of practice which we recommend should be reviewed as appropriate to take account of the guidance given in this report (see also para 27). We also refer in Appendix F to containment facilities in high security isolation units.

The implementation of preventive measures

8 The committee are aware that the regulation of microbiological safety can only command the respect of both scientists and the public if it is soundly based, and also that the safety measures proposed must be reasonably practicable and that the costs in time, money or effort should be balanced against the risks.

9 Since the HSW Act became law, it has been generally accepted that agreed standards for any work activity are desirable rather than that every argument be settled at works level without a standard which can be used for reference. There has been some confusion however among workers in microbiology about which standards to adopt because of the differing nomenclature used by the various committees for containment measures and for the categorisation of pathogens. This will now be avoided if the classification of pathogens and the levels of containment described here are adopted as the basic standard for all microbiological work. The model code of practice is intended to form the basis on which local and national users can prepare any further guidance they may require in detail for work of a special nature.

10 A distinction is intended throughout this document between the use of 'must' which indicates an essential requirement and the use of 'should' which indicates our strong recommendation.

11 An understanding by all concerned of the principles of occupational health and safety and the continual application of the detail set out in local codes of practice are essential if safe working is to be achieved and maintained. We recommend that this report be read in conjunction, as appropriate to the work, with standard texts some of which are listed together with other sources of useful information in the reference section (page 48). The needs and resources for training are dealt with in Appendix I.

Future work

12 Several research projects should be undertaken to help in future decisions, as follows:

- (a) we need to know in quantitative terms the effect of precautions such as those we recommend in reducing contamination of the worker. If the figures were known, alternative methods could be compared. They would also provide a partial basis for further efforts to make quantitative risk assessments;
- (b) as indicated in the Howie Report⁴, we need to have more adequate epidemiological records of the type and number of infections occurring with details of the laboratory and the work being done; this might form part of a more general study including other occupations;
- (c) there should be continuing surveillance and reporting of safety practices in laboratories. Correlation of these findings by a central body would allow periodic reviews of hazard and associated risks from work with pathogens to be made and publicised.

Categories of pathogens

Definition of hazard groups

13 The classification of pathogens in this report is based on the inherent hazard of the organism. The corresponding levels of containment set out in the model code of practice are intended to compensate for microbiological risks encountered when working with pathogens as defined in the various hazard groups. Hazard is taken as expressing the degree of danger associated with the inherent nature of the organism and the risk as the probability that in certain given circumstances the dangers will become expressed and result in infection. In general the more serious the disease, the greater the hazard. The more likely that infection will occur, the higher the risk. In reality there are many grades of risk arising from work with pathogens dependent on such factors as the immune status of the individual or community and the dose, route and site of infection. We have therefore in certain cases suggested modification to the recommendations and requirements set out in the model code of practice at the various levels of containment.

14 We have classified micro-organisms into four hazard groups which are defined below according to the following criteria:

- (a) is the organism pathogenic for man?
- (b) is it a hazard to laboratory workers?
- (c) is it transmissible in the community?
- (d) is effective prophylaxis and treatment available?

Hazard groups**

GROUP 1 An organism that is most unlikely to cause human disease.

GROUP 2 An organism that may cause human disease and which might be a hazard to laboratory workers but is unlikely to spread in the community. Laboratory exposure rarely produces infection and effective prophylaxis or effective treatment are usually available.

GROUP 3 An organism that may cause severe human disease and present a serious hazard to laboratory workers. It may present a risk of spread in the community but there is usually effective prophylaxis or treatment available.

GROUP 4 An organism that causes severe human disease and is a serious hazard to laboratory workers. It may present a high risk of spread in the community and there is usually no effective prophylaxis or treatment.

Allocation of pathogens to hazard groups

15 In the following tables organisms are assigned according to the infective hazard they pose for healthy laboratory workers to one of the three higher hazard groups. This categorisation does not allow for any additional risk that an organism may present for those persons with pre-existing disease, compromised immunity or who are pregnant, nor does it take account of the allergenic properties of the organisms or of toxic hazards from their products; microbial toxins are considered to come within the scope of precautions appropriate to hazardous chemicals.

16 The number of the hazard group of a particular organism matches that of the level of containment under which it must be handled (see paras 22 to 43); where modifications to this containment level have been considered justified, they

* Zoonotic organisms are included in the hazard groups primarily on the basis of the hazard to humans. It should be noted that zoonotic and other animal and poultry pathogens may cause serious or epidemic disease in the animal and poultry populations and for that reason work with such pathogens must be conducted under appropriate containment conditions. Advice concerning legislation controlling animal and poultry pathogens and also pathogens of plants and fish, may be obtained from the Agriculture and Fisheries departments (see 'Pathogens controlled by the Agricultural and Fisheries departments' Appendix J).

† For the purposes of this report organisms in hazard groups 2, 3 and 4 are referred to as pathogens.

are described in footnotes to the tables and designated by symbols following the number of the hazard group in the lists of organisms. Only organisms in hazard groups 2, 3 and 4 are listed; their names are those in current usage in the UK. Many have one or more synonyms and before assuming that an unlisted organism is categorised as hazard group 1, the laboratory worker must verify that its name is not synonymous with that of an organism already listed. For this purpose, we have suggested in the reference section some publications: for bacteria^{7,8,9}; for fungi¹⁰; for viruses¹¹; and for parasites¹². Names in inverted commas do not appear on the *Approved Lists*⁶ and have no official standing in bacterial nomenclature. Organisms that are not listed should be categorised according to the hazard assessment made by the person identified as responsible for the work in question (see para 24) in consultation with the local safety committee⁷; advice will be provided by HSE if requested (see para 27).

17 It should be noted that particular strains of listed organisms may require a category different from that given. Examples are mutants of increased or decreased virulence or genetically manipulated organisms, attenuated vaccine viruses or bacteria and antibiotic resistant strains e.g. plasmid borne. A single category has been used where taxonomy is such that many organisms can be grouped together, e.g. *Salmonella* spp, *Streptococcus* spp, and where it would not be practical to list and classify every organism. In these cases different degrees of containment may be needed depending on the findings of a properly conducted hazard/risk assessment (see para 26). It should also be noted that some organisms are pathogens of veterinary or agricultural importance, or are pathogens of fish, work with which is subject to regulation by the Agriculture and Fisheries departments (see 'Pathogens controlled by the Agriculture and Fisheries departments' Appendix J).

Bacteria, Chlamydia, Rickettsiae and Mycoplasmas

To be read in conjunction with containment levels in the model code of practice

18 The categorisation of bacteria, chlamydia, rickettsiae and mycoplasmas is listed below.

<i>Acinetobacter calcoaceticus</i>	2	<i>Clostridium tetani</i>	2V
<i>Acinetobacter lwoffii</i>	2	<i>Clostridium</i> other spp (except those	
" <i>Actinobacillus actinoides</i> "	2	known to be non pathogenic)	2
<i>Actinobacillus actinomycetem-</i>		<i>Corynebacterium diphtheriae</i>	2V
<i>comitans</i>	2	" <i>Corynebacterium haemolyticum</i> "	2
<i>Actinobacillus lignieresii</i>	2	" <i>Corynebacterium minutissimum</i> "	2
<i>Actinobacillus suis</i>	2	" <i>Corynebacterium ulcerans</i> "	2
<i>Actinomadura</i> spp	2	<i>Coxiella burnetii</i>	3
<i>Actinomyces bovis</i>	2	<i>Edwardsiella tarda</i>	2
<i>Actinomyces israelii</i>	2	<i>Eikenella corrodens</i>	2
<i>Aeromonas hydrophila</i>	2	<i>Enterobacter aerogenes</i>	2
<i>Arizona</i> spp	2	<i>Erysipelothrix rhusiopathiae</i>	
<i>Bacillus anthracis</i>	3(v)	("insidiosus")	2
<i>Bacillus cereus</i>	2	<i>Escherichia coli</i> (except genetically	
<i>Bacterionemia matruchottii</i>	2	crippled strains)	2
<i>Bartonella bacilliformis</i>	2	<i>Flavobacterium meningosepticum</i>	2
<i>Bordetella parapertussis</i>	2	<i>Francisella tularensis</i> (Type A)	3(v)
<i>Bordetella pertussis</i>	2	<i>Francisella tularensis</i> (Type B)	2
<i>Borrelia</i> - all spp	2	<i>Haemophilus</i> spp	2
<i>Brucella</i> spp	3	" <i>Kingella kingae</i> "	2
<i>Campylobacter</i> spp	2	<i>Klebsiella</i> spp	2
<i>Cardiobacterium hominis</i>	2	<i>Legionellaceae</i>	2
<i>Chlamydia psittaci</i> (avian strains only)	3	<i>Leptospira interrogans</i> ("ictero-	
<i>Chlamydia</i> (other strains)	2	<i>haemorrhagiae</i> ") all serovars	2G
<i>Clostridium botulinum</i>	2(v)	<i>Listeria monocytogenes</i>	2

* Safety Representatives and Safety Committees Regulations 1977.

<i>Moraxella</i> spp	2	<i>Rickettsia canada</i>	3
<i>Mycobacterium africanum</i>	3V	<i>Rickettsia conorii</i>	3
<i>Mycobacterium avium</i>	2	" <i>Rickettsia montana</i> "	3
<i>Mycobacterium bovis</i> (excluding BCG strain)	3V	" <i>Rickettsia mooseri</i> "	3
<i>Mycobacterium bovis</i> (BCG strain)	2	<i>Rickettsia prowazeki</i>	3
<i>Mycobacterium chelonae</i>	2	<i>Rickettsia rickettsii</i>	3
<i>Mycobacterium fortuitum</i>	2	<i>Rickettsia sennetsu</i>	3
<i>Mycobacterium intracellulare</i>	3	<i>Rickettsia tsutsugamushi</i>	3
<i>Mycobacterium kansasii</i>	3	<i>Rochalimaea quintana</i>	3
<i>Mycobacterium leprae</i>	3	Vole rickettsia	3
<i>Mycobacterium malmoeense</i>	3	" <i>Salmonella paratyphi A</i> "	3
<i>Mycobacterium marinum</i>	2	<i>Salmonella typhi</i>	3v
<i>Mycobacterium scrofulaceum</i>	2	<i>Salmonella</i> (other spp)	2
<i>Mycobacterium simiae</i>	2	<i>Serratia liquefaciens</i>	2
<i>Mycobacterium szulgai</i>	3	<i>Serratia marcescens</i>	2
<i>Mycobacterium tuberculosis</i>	3V	<i>Shigella dysenteriae</i> (Type 1)	3
<i>Mycobacterium ulcerans</i>	2	<i>Shigella</i> (other spp)	2
<i>Mycobacterium xenopi</i>	2	<i>Staphylococcus aureus</i>	2
<i>Mycoplasma pneumoniae</i>	2	<i>Streptobacillus moniliformis</i>	2
<i>Neisseria</i> spp	2	<i>Streptococcus</i> spp (Lancefield Groups A, B, C, D, G)	2
<i>Nocardia asteroides</i>	2	<i>Streptococcus</i> other spp (except those known to be non pathogenic)	2
<i>Nocardia brasiliensis</i>	2	<i>Treponema pallidum</i>	2G
" <i>Noguchia granulosis</i> "	2	<i>Treponema pertenue</i>	2G
<i>Pasteurella</i> spp	2	<i>Vibrio cholerae</i> (incl <i>El Tor</i>)	2
<i>Plesiomonas shigelloides</i>	2	<i>Vibrio parahaemolyticus</i>	2
<i>Proteus</i> spp	2	<i>Yersinia enterocolitica</i>	2
<i>Providencia</i> spp	2	<i>Yersinia pseudotuberculosis</i>	3v
<i>Pseudomonas mallei</i>	3	<i>Yersinia pestis</i> (<i>Y. pestis</i>)	3v
<i>Pseudomonas pseudomallei</i>	3	<i>Yersinia pseudotuberculosis</i>	2
<i>Pseudomonas</i> other spp	2		
<i>Rickettsia akari</i>	3		

Modifications to containment level in the model code of practice.

- G = gloves must be used
V = vaccination required (unless known to be immune)
v = vaccination recommended (unless known to be immune)
(v) = vaccine available, use discretionary

Fungi

To be read in conjunction with containment levels in the model code of practice

19 This categorisation is restricted to fungi which may pose a hazard for healthy persons (see para 15). Fungi which infect following traumatic inoculation e.g. *Madurella mycetomatis*, *Phialophora verrucosa*, together with a large number of fungi normally saprophytic but which cause infections in the compromised host, are excluded. Unless otherwise stated, all fungi from clinical specimens must be handled at containment level 2.

<i>Aspergillus fumigatus</i>	2	<i>Epidermophyton floccosum</i>	2
<i>Blastomyces dermatitidis</i>	3	<i>Histoplasma</i> spp	3
<i>Candida albicans</i>	2	<i>Microsporium</i> spp	2
<i>Coccidioides immitis</i>	3	<i>Paracoccidioides brasiliensis</i>	3
<i>Cryptococcus neoformans</i>	2	<i>Sporothrix schenckii</i>	2
(<i>Filobasidiella neoformans</i>)	2S	<i>Trichophyton</i> spp	2

Modifications to containment level in the model code of practice.

- S = A microbiological safety cabinet must be used

Parasites

To be read in conjunction with containment levels in the model code of practice

20 The categorisation of parasites is listed below. The allocation to hazard groups is that indicated by the degree of hazard presented by the infective stage(s) of each parasite. Preparations which are known to be free of infectious stages may not require this level of containment (see para 27).

<i>Acanthamoeba</i> spp (especially <i>A. culbertsoni</i>)	2S	<i>Mansonella ozzardi</i>	2
<i>Ancylostoma duodenale</i>	2G	<i>Necator americanus</i>	2G
<i>Angiostrongylus</i> spp	2	<i>Naegleria</i> spp (especially <i>fowleri</i>)	3
<i>Ascaris lumbricoides</i>	2	<i>Onchocerca volvulus</i>	2
<i>Babesia microti</i>	2	<i>Opisthorchis</i> spp	2
<i>Babesia divergens</i>	2	<i>Paragonimus westermani</i>	2
<i>Balantidium coli</i>	2	<i>Plasmodium</i> (human & simian)	2
<i>Brugia</i> spp	2	<i>Pneumocystis carinii</i>	2
<i>Capillaria</i> spp	2	<i>Schistosoma haematobium</i>	2G
<i>Clonorchis sinensis</i>	2	<i>Schistosoma mansoni</i>	2G
<i>Dipetalonema streptocerca</i>	2	<i>Schistosoma japonicum</i>	2G
<i>Dipetalonema perstans</i>	2	<i>Schistosoma intercalatum</i>	2G
<i>Diphyllobothrium latum</i>	2	<i>Strongyloides</i> spp	2
<i>Dracunculus medinensis</i>	2	<i>Taenia saginata</i>	2
<i>Echinococcus</i> spp	3&P	<i>Taenia solium</i>	2
<i>Entamoeba histolytica</i>	2	<i>Toxocara canis</i>	2
<i>Fasciola hepatica</i>	2	<i>Toxoplasma gondii</i>	3&P
<i>Fasciola gigantica</i>	2	<i>Trichinella</i> spp	2
<i>Fasciolopsis buski</i>	2	<i>Trichomonas vaginalis</i>	2
<i>Giardia lamblia</i>	2	<i>Trichostrongylus</i> spp	2
<i>Hymenolepis nana</i> (human origin)	2	<i>Trichuris trichiura</i>	2
<i>Hymenolepis diminuta</i>	2	<i>Trypanosoma cruzi</i>	3
<i>Leishmania</i> (mammalian) spp	3&P	<i>Trypanosoma brucei</i> sub-spp	2
<i>Loa loa</i>	2	<i>Wuchereria bancrofti</i>	2

Modifications to containment level in the model code of practice.

G	=	gloves must be used
S	=	a microbiological safety cabinet must be used
&	=	a microbiological safety cabinet is not essential
P	=	the laboratory need not be sealable for fumigation and a continuous inward airflow during work is not essential

Viruses

To be read in conjunction with containment levels in the model code of practice

21 All viruses found in man which are not listed below are assigned to hazard group 2.

Arenaviridae		Unassigned Bunyaviruses	
Lymphocytic choriomeningitis virus		Hantaan, Korean haemorrhagic fever, epidemic nephro-nephrosis viruses	3
(LCM) neurotropic strains	3		
Junin, Lassa, Machupo and Mopeia viruses	4	"Filoviridae"	
		Ebola, Marburg viruses	4
Bunyaviridae		Hepatitis B virus	
Group C		(virus of serum hepatitis)	3**(v)
Oropouche virus	3	Herpesviridae	
Phleboviruses		B virus of monkeys	
Rift Valley fever virus	3 ^a V	(<i>Herpesvirus simiae</i>)	3*
Nairoviruses		Herpes simplex virus	
Congo, Crimean haemorrhagic fever viruses, Hazara	4	(Herpes febrilis, herpes genitalis,	
		<i>Herpesvirus hominis</i>)	2gE

Orthomyxoviridae			Alphaviruses	
Influenza virus recent isolates	2 ^s S		Eastern equine encephalo-myelitis virus	3 ^a
			Venezuelan equine encephalo-myelitis virus	3 ^a (v)
Paramyxoviridae			Western equine encephalo-myelitis virus	3 ^a
Newcastle disease virus	2 ^a E		Flaviviruses	
Measles virus	2v		Yellow fever virus	3V
Mumps virus	2v		Japanese B encephalitis,	
			Murray Valley encephalitis	
Picornaviridae			(Australia encephalitis),	
Poliovirus 1,2,3	2V		Rocio, St Louis encephalitis viruses	3
Poxviridae			Tick-borne viruses	
Variola (major & minor) virus	4V		Kyasanur Forest disease, Omsk	
Whitepox virus	4V		haemorrhagic fever disease viruses	
Vaccinia	2V		Absettarov, Hanzalova, Hypr,	
Monkey pox virus	3V		Russian spring-summer encephalitis	
All other members	2 ^a G		viruses	4V
Retroviridae			Kumlinge	3
Human T-Cell Leukaemia viruses	3		Powassan virus	3
			Louping ill virus	2(v)
Rhabdoviridae			Tick-borne encephalitis	2(v)
Rabies virus	3 ^a V		Unclassified viruses	
Vesicular stomatitis virus	2 ^a s		Hepatitis (non-A-non-B) viruses	2 ^{**}
Togaviridae			Unconventional agents	
Rubivirus			Kuru and Creutzfeldt-Jakob agents	2S ^b G
(Rubella virus)	2v			

Modifications to containment level in the model code of practice.

- E = eye protective equipment must be used
- G = gloves must be used
- g = gloves recommended
- V = vaccination required (unless known to be immune)
- v = vaccination recommended (unless known to be immune)
- (v) = vaccine available, use discretionary
- S = a microbiological safety cabinet must be used
- s = a microbiological safety cabinet is recommended
- * = see Appendix C
- / = see Appendix G
- ** = see Appendix H
- a = see Appendix J
- b = see report of the Advisory Group on the Management of Patients with Spongiform Encephalopathy, HMSO, November 1981

Categories of containment

Model code of practice

22 This section sets out the essential elements of a model code of practice for microbiological safety. It defines four physical containment levels suitable for work with organisms in each of four hazards groups, e.g. a pathogen in hazard group 2 must be handled at containment level 2, but reference should be made to the list of pathogens in paras 18–21 where modifications to the containment requirements for certain pathogens are described, and to paragraph 27.

23 The model code is intended to form the basis on which local and national users can prepare their codes of practice and any further guidance that may be required in greater detail for work of a special nature, e.g. in research, teaching or industrial establishments.

24 Under the HSW Act employers are required to issue a general statement of their policy on health and safety and to specify in writing the organisation and arrangements to implement this policy. In each establishment the person(s) responsible for the work or particular aspects of work which involve microbiological hazard must be identified. Each establishment must draw up a local code of practice in consultation with the local safety committee and the safety representatives*. The local code must include information on such matters as:

- (a) selection and training of laboratory staff and supervision of work;
- (b) policy for disinfection and procedures for the disposal of potentially infective material;
- (c) guidance for ancillary and maintenance staff, contractors and visitors;
- (d) maintenance and test procedures for the ventilation system, high efficiency particulate air (HEPA) filters, microbiological safety cabinets and other safety equipment;
- (e) medical surveillance, which should include screening procedures including the immune status of the individual, sickness investigation, issue of medical contact cards, immunisation procedures, maintenance of baseline serum samples from staff;
- (f) the duties of the safety officer.

25 It should be noted that the HSW Act places wider responsibilities on employers and employees than those which relate to microbiological hazards. The local code must therefore take account of other regulations and codes, e.g. those relating to the use of radio isotopes and toxic and dangerous chemicals, also fire precautions which should be agreed with the local fire officers.

26 The person(s) identified as responsible for the work in question (para 24) must assess, in consultation with the local safety committee* and safety adviser at each establishment, the microbiological risks that might arise during work and should take into account such factors as:

- (a) the virulence and transmissibility of the organisms;
- (b) the titre or concentration of the organisms in the materials to be handled;
- (c) the scale and type of work and the possible effects of these on the extent of dissemination of the organisms.

27 Work with pathogens and materials known to contain them must be conducted at the appropriate containment level indicated in the model code of practice, but the level may be altered to provide more stringent containment conditions depending upon the local assessment of risk. Less stringent conditions must not be adopted before a full risk assessment has been made and agreed by the local safety committee,* and in the case of group 3 and 4 pathogens until

* Safety Representatives and Safety Committees Regulations 1977.

consultation with the HSE has taken place. The requirements of the Health and Safety (Dangerous Pathogens) Regulations 1981 apply to those pathogens listed in Schedule 1 of the Regulations*.

28 It is recognised that there are special problems for clinical diagnostic laboratories. The minimum containment requirement is level 2 (see paragraphs 3 and 7).

Laboratory containment levels

29 For the purposes of this model code the terms listed below have the following meaning:

- (a) laboratory: the room in which the organisms are handled;
 - (b) laboratory suite: one or more laboratories, not necessarily of the same discipline, and ancillary rooms within a Section or Department with shared use of facilities such as autoclaves, centrifuges, etc;
 - (c) laboratory unit: a separate building, or self-contained suite within a building, containing one or more laboratories and with ancillary rooms such as airlocks, changing rooms, showers, autoclave room, etc.
- 30 A tabular summary of the main requirements for each containment level is given in page 15.

Containment level 1

31 Containment level 1 is suitable for work with organisms in hazard group 1. Laboratory personnel must receive instruction in the procedures conducted in the laboratory.

- 1 The laboratory should be easy to clean. Bench surfaces should be impervious to water and resistant to acids, alkalis, solvents and disinfectants.
- 2 If the laboratory is mechanically ventilated, an inward air flow into the laboratory should be maintained by extracting room air to atmosphere.
- 3 The laboratory must contain a wash hand basin or sink that can be used for hand washing.
- 4 The laboratory door should be closed when work is in progress.
- 5 Laboratory coats or gowns should be worn in the laboratory and removed when leaving the laboratory suite.
- 6 Eating, chewing, drinking, smoking, storing of food and applying cosmetics must not take place in the laboratory.
- 7 Mouth pipetting must not take place.
- 8 Hands must be disinfected or washed immediately when contamination is suspected, after handling viable materials, and also before leaving the laboratory.
- 9 All procedures must be performed so as to minimise the production of aerosols.
- 10 Effective disinfectants must be available for immediate use in the event of spillage.
- 11 Bench tops should be cleaned after use.
- 12 Used laboratory glassware and other materials awaiting disinfection must be stored in a safe manner. Pipettes, if placed in disinfectant, must be totally immersed.

* Schedule 1. List of pathogens the keeping or handling of which is to be notified to the HSE: Crimean Haemorrhagic Fever virus (Congo); Ebola virus; Junin Haemorrhagic Fever virus; Lassa Fever virus; Machupo Haemorrhagic Fever virus; Marburg virus; Rabies virus; Simian Herpes B virus; Smallpox virus; Venezuelan Equine Encephalitis virus.

- 13 All waste material which is not to be incinerated should be rendered non-viable before disposal.
- 14 Materials for disposal must be transported without spillage in robust containers.
- 15 All accidents and incidents must be recorded.

Containment level 2

32 Containment level 2 is suitable for work with pathogens in hazard group 2. Laboratory personnel must receive instruction and training in handling pathogens and an appropriate standard of supervision of the work must be maintained.

- 1 The laboratory should be easy to clean. Bench surfaces should be impervious to water and resistant to acids, alkalis, solvents and disinfectants.
- 2 Access to the laboratory should be limited to laboratory personnel and other specified persons.
- 3 There should be adequate space (24 m³) in the laboratory for each worker.
- 4 If the laboratory is mechanically ventilated, an inward airflow into the laboratory must be maintained by extracting room air to atmosphere.
- 5 The laboratory must contain a wash hand basin which should be located near the laboratory exit. Taps must be of a type which can be operated without being touched by hand.
- 6 An autoclave for the sterilisation of waste materials must be readily accessible, normally in the same building as the laboratory.
- 7 The laboratory door should be closed when work is in progress.
- 8 Laboratory coats or gowns, which should be side or back fastening, must be worn in the laboratory and removed when leaving the laboratory suite. Separate storage (e.g. pegs) must be provided in the laboratory suite for this clothing.
- 9 Eating, chewing, drinking, smoking, storing of food and applying cosmetics must not take place in the laboratory.
- 10 Mouth pipetting must not take place.
- 11 Hands must be disinfected or washed immediately when contamination is suspected, after handling infective materials, and also before leaving the laboratory.
- 12 In general, work may be conducted on the open bench, but care must be taken to minimise the production of aerosols. For manipulations such as vigorous shaking or mixing and ultrasonic disruption etc, a microbiological safety cabinet (class I; BS 5726: 1979) or equipment which is designed to contain the aerosol must be used. The cabinet must exhaust to the outside air or to the laboratory air extract system, (see para 34, 14(b)).
- 13 Effective disinfectants must be available for routine disinfection and immediate use in the event of spillage.
- 14 Bench tops must be disinfected after use.
- 15 Used laboratory glassware and other materials awaiting sterilisation must be stored in a safe manner. Pipettes, if placed in disinfectant, must be totally immersed.
- 16 Material for autoclaving must be transported to the autoclave without spillage in robust containers.
- 17 All waste materials must be made safe before disposal or removal to the incinerator.

- 18 All accidents and incidents must be immediately reported to and recorded by the person responsible for the work.

Diagnostic laboratories

33 All clinical microbiological suites must contain a microbiological safety cabinet (class I; BS 5726: 1979, or one with an equivalent protection factor). In veterinary practice, a class I safety cabinet will not be required if diagnostic work is limited to the examination of fixed slides which have been prepared and fixed elsewhere.

Containment level 3

34 Containment level 3 is suitable for work with pathogens in hazard group 3. Laboratory personnel must have had training in handling pathogenic and potentially lethal organisms, also in the use of safety equipment and controls. A high standard of supervision of the work must be maintained.

- 1 The laboratory must be easy to clean. Bench surfaces and the floor must be impervious to water and resistant to acids, alkalis, solvents and disinfectants.
- 2 The laboratory must be sealable to permit fumigation.
- 3 There must be adequate space (24m³) in the laboratory for each worker.
- 4 The laboratory should be sited in an area away from general circulation. Access to the laboratory must be limited to authorised personnel. The laboratory door must be locked when the room is unoccupied.
- 5 A specific biohazard sign must be posted at the entry to the laboratory and the door must contain a glass panel so that the occupants can be seen.
- 6 A continuous airflow into the laboratory must be maintained during work with pathogens by one of the following means:
 - (a) extracting the laboratory air through independent ducting to the outside air through a HEPA filter;
 - (b) extracting the laboratory air to the outside air with a fan and HEPA filter sited in a wall or window of the laboratory;
 - (c) ducting the exhaust air from a microbiological safety cabinet to the outside air through a HEPA filter;
 - (d) a safe variation of these provisions. Provisions should also be made for comfort factors e.g. fresh-air, temperature control.

In laboratories which have a mechanical air supply system, the supply and extract airflow must be interlocked to prevent positive pressurisation of the room in the event of failure of the extract fan. The ventilation system must also incorporate a means of preventing reverse airflows.

- 7 A wash hand basin must be provided near the exit of the laboratory. Taps must be of a type which can be operated without being touched by hand.
- 8 An autoclave for sterilisation of waste materials should be situated preferably within the laboratory, but one must be readily accessible in the laboratory suite.
- 9 Laboratory doors must be kept closed when work is in progress.
- 10 Side or back fastening gowns must be used in the laboratory and they must be autoclaved before removal for laundering. These gowns must not be used outside the laboratory suite.
- 11 Gloves must be worn for all work with infective materials and the hands must be washed before leaving the laboratory.

- 12 Eating, chewing, drinking, smoking, storing of food and applying cosmetics must not take place in the laboratory.
- 13 Mouth pipetting must not take place.
- 14
 - (a) All laboratory procedures with infective materials must be conducted in a microbiological safety cabinet (class I or class III BS 5726: 1979, or unit with equivalent protection factor or performance) except where the equipment to be used provides containment of the potential aerosol.
 - (b) The cabinet must exhaust through a HEPA filter to the outside air or to the laboratory air extract system, and in other respects such as siting, performance, protection factor and air filtration, it must comply with the specifications detailed in BS 5726: 1979. When laboratories are faced with a major problem because of difficulties in arranging for the cabinet to exhaust to the open air, recirculation of exhaust air through two HEPA filters in series may in exceptional circumstances be considered as an alternative. In these cases the maintenance of a continuous airflow into the laboratory during work with pathogens (see 34(6) (a) and (b)) will be of particular importance and such an option must not be adopted without prior consultation with the HSE.
- 15 The laboratory should contain its own equipment e.g. centrifuge in which sealed buckets must be used, incubator, refrigerator, deep-freeze, vapour phase liquid nitrogen chest etc so that all infective group 3 pathogenic materials are held within the laboratory and nowhere else. Where this is not reasonably practicable (see para 27) material must be transported and stored without spillage in properly labelled robust containers which must be opened only in containment level 3 accommodation.
- 16 Effective disinfectants must be available for routine disinfection and immediate use in the event of spillage.
- 17 Materials for autoclaving must be transported in robust containers without spillage to the autoclave.
- 18 All waste materials must be made safe before disposal or removal to the incinerator.
- 19 All accidents, spills and exposures to infective materials must be immediately reported to and recorded by the person responsible for the work.

Containment level 4

- 35 Containment level 4 is suitable for work with pathogens in hazard group 4. A specific code of practice must be prepared for the work in the laboratory and a safety officer (accountable to the person identified as responsible for the work in question) must be appointed. Personnel must be over the age of 18 and must have had specific training in the working of the laboratory and the use of safety equipment and must receive specific training, instruction and information in the handling of the pathogen(s) concerned. The work must be supervised.
 - 1 The laboratory unit must be designed so that it is easily cleaned. Bench surfaces, walls, floors and ceiling must be impervious to water and resistant to acids, alkalis, solvents and disinfectants.
 - 2 The laboratory unit must be sealable to permit fumigation.
 - 3 There must be adequate space (24m³) in the laboratory working area for each worker.
 - 4 The laboratory unit must be a separate building or form an isolated part of a building. Access must be restricted to authorised personnel and a key procedure established so that entry is restricted at all times.
 - 5 Entry must be through an airlock. The clean side of the airlock must be

separated from the restricted side by changing and showering facilities and preferably by interlocking doors. The outer door must be labelled with a 'work in progress' sign.

- 6 The laboratory unit must be ventilated through independent ducting by a plenum and a total-loss exhaust air system. The exhaust air must be filtered through two HEPA filters mounted in series before it leaves the laboratory unit. The input air must be filtered through a single HEPA filter. At all times, the airflow must be from the outside area into the laboratory. A negative pressure of 7 mm of water must be maintained in the laboratory and a negative pressure of about 3 mm of water in the airlock. An alarm system must be fitted to detect any unacceptable change in air pressure and manometers must be displayed which can be read from both inside and outside the laboratory.
- 7 The supply and extract airflow must be interlocked to prevent positive pressurisation of the laboratory in the event of failure of the extract fan and an emergency source of electric supply must be provided to cut in automatically in the event of a power failure. The ventilation system must incorporate a means of preventing reverse airflows.
- 8 An additional ventilated airlock that can be fumigated may be required for passage of equipment which cannot enter the laboratory unit through the personnel airlock or autoclave.
- 9 At all times during work in the laboratory unit, there must be a second competent person available to assist in the case of an emergency. An observation window, or suitable alternative, must be installed in the laboratory so that the occupants can be seen.
- 10 Eating, chewing, drinking, smoking, storing of food and applying cosmetics must not take place in the laboratory.
- 11 Mouth pipetting must not take place.
- 12 A complete change of clothing must be worn in the laboratory unit. The clothing must be removed after work in the dirty side of the changing area and placed in a container for autoclaving. A shower must be taken before leaving the laboratory unit.
- 13 High performance respiratory protective equipment (two or more units) (see Appendix B), must be available in the clean side of the laboratory unit for use in an emergency.
- 14 All effluent, including that from the shower, must be rendered safe.
- 15 A double-ended autoclave with interlocking doors with entry in the laboratory and exit in a clean area must be provided.
- 16 There must be a telephone or other means of outside communication inside the laboratory unit.
- 17 All laboratory procedures with infective materials must be conducted in a class III microbiological safety cabinet (BS 5726: 1979, or one with equivalent performance). The exhaust from the cabinet must pass through two HEPA filters mounted in series before ducting to the outside air or to the laboratory air extract system.
- 18 Effective disinfectants must be available for immediate use.
- 19 All infective group 4 pathogenic material must be stored in the laboratory unit and nowhere else.
- 20 All material must be made safe before being removed from the laboratory unit. A double-ended dunk tank filled with an effective disinfectant, or an alternative safe system, may be required for the removal of materials which cannot be autoclaved. Removal of material in this manner, also materials

removed through the equipment airlock, must be undertaken only with authorisation of the safety officer and under conditions defined in the local code of practice. The dunk tank should be sealed during fumigation if the disinfectant is incompatible with the fumigant.

- 21 An efficient insect and rodent control programme must be in operation.
- 22 All accidents, spills and accidental exposures to infective materials must be immediately reported to and recorded by the safety officer who must take the appropriate measures specified in the local code of practice.

Diagnostic laboratories

- 36 Where it is intended to propagate a hazard group 4 pathogen, full containment level 4 must be used. If other tests are required on such material it may be possible to use alternative containment levels (see Appendix E).

Tabular summary of laboratory containment requirements

Containment requirements	Containment levels			
	1	2	3	4
Laboratory site: isolation	No	No	Partial	Yes
Laboratory: sealable for fumigation	No	No	Yes	Yes
Ventilation: inward airflow/negative pressure through safety cabinet	Optional	Optional	Yes	Yes
	No	Optional	Optional	No
	No	No	Optional	No
	No	No	Optional	Yes
Airlock	No	No	Optional	Yes
	:with shower	No	No	Yes
Wash hand basin	Yes	Yes	Yes	Yes
Effluent treatment	No	No	No	Yes
Autoclave site:	on site	No	No	No
	in suite	No	Yes	No
	in lab: free standing	No	Optional	No
	in lab: double-ended	No	No	Yes
Microbiological safety cabinet/enclosure	No	Optional†	Yes	Yes
Class of cabinet/enclosure*	—	class I	class I/III	class III

* Guidance on the use of class II microbiological safety cabinets is given in Appendix A

† Required for clinical microbiological suites.

Animal room containment levels

37 The following four physical containment levels are suitable for work with vertebrates* which are deliberately inoculated with organisms in each of the four hazard groups or with viable materials suspected of containing these organisms†. The animal accommodation should also comply with the requirements in the relevant regulations (The Cruelty to Animals Act 1876) and in guidelines such as the guidance notes on the Law Relating to Experiments on Animals in Great Britain (Research Defence Society and Home Office, July 1974).

38 For the purpose of this model code, the terms listed below have the following meaning:

- (a) animal room: the room in which the animals are held;
- (b) animal suite: one or more animal rooms with an anteroom and other ancillary rooms separated from general corridors and service areas;
- (c) animal unit: a building, or separate area within a building, containing animal rooms and other facilities such as changing rooms, showers, autoclave, animal food stores, etc.

39 Animals infected experimentally with organisms in the four hazard groups may be small e.g. mice or large e.g. farm animals. The requirements for maintenance of the animals may differ in scale therefore, but the basic principles for microbiological safety will be similar. This model code sets out those principles which should be expressed in detail in a local code of practice (see also para 24).

* Guidance on the physical containment suitable for work with invertebrates is given in Appendix D.

† It is recognised that animals can harbour infectious organisms which are acquired naturally. These infections can give rise to a chronic carrier state, or the agent might persist in a latent non-infective form which can be reactivated periodically or as a result of certain stimuli. If the possibility that such an agent may be excreted by an animal during the course of an experiment cannot be excluded, the animal should be kept at a containment level appropriate to the risk (see Appendix C).

Animal containment level 1

40 Personnel must receive training in the handling of the animals to be used. The person responsible for the animal experiment must ensure that all those having contact with the animals and waste materials are familiar with the local code of practice and are aware of any other precautions and procedures that may be required.

- 1 The animal room should be easy to clean.
- 2 The animal room must be adequately ventilated.
- 3 Access to the room must be limited to authorised persons.
- 4 An autoclave for the sterilisation of waste materials should be available on site.
- 5 Hands must be disinfected or washed immediately when contamination is suspected and after handling animals or animal waste.
- 6 Suitable protective clothing and footwear should be worn in the animal room and cleansed, or removed, when leaving the animal room.
- 7 Eating, chewing, drinking, smoking, storing of food for human consumption and applying cosmetics must not take place in the animal room.
- 8 Mouth pipetting must not take place.
- 9 All procedures should be performed so as to minimise the production of aerosols.
- 10 Effective disinfectants must be available for immediate use.
- 11 All waste materials must be disposed of safely.
- 12 Used animal cages must be rendered non-infective after use.
- 13 Materials for autoclaving or incineration, also used animal cages, must be transported without spillage.
- 14 All accidents, including animal bites and scratches, must be reported and recorded.

Animal containment level 2

41 Animal containment level 2 is suitable for work with vertebrates which are deliberately inoculated with organisms in hazard group 2 (or viable material suspected of containing these organisms). Personnel must receive training in the handling of the animals to be used and an appropriate standard of supervision of the work must be maintained. The person responsible for the animal experiment must ensure that all those having contact with the animals and waste materials are familiar with the local code of practice and are aware of any other precautions and procedures that may be required.

- 1 The animal room should be easy to clean. If floor drains are installed, the drain traps should always contain water. Drain traps must regularly be disinfected and cleaned.
- 2 The animal room must be adequately ventilated and, where mechanical ventilation is used, an inward airflow into the room should be maintained by extracting room air to atmosphere.
- 3 The animal room door must be closed when infected animals are present and it should be labelled with a sign indicating the level of work.
- 4 Access to the animal room must be limited to authorised persons.
- 5 An autoclave and/or an incinerator for the sterilisation of waste materials must be available on site.

- 6 Hands must be disinfected or washed immediately when contamination is suspected and after handling animals or animal waste.
- 7 Facilities must be provided for hand washing preferably in the animal room but if this is impracticable in an adjoining area.
- 8 Suitable protective clothing and footwear must be worn in the animal room and cleansed or removed when leaving the room.
- 9 Eating, chewing, drinking, smoking, storing of food for human consumption and applying cosmetics must not take place in the animal room.
- 10 Mouth pipetting must not take place.
- 11 All manipulations must be performed so as to minimise the production of aerosols. For procedures such as harvesting of infected tissues and fluids where significant aerosols may be created, a microbiological safety cabinet (class 1 BS 5726: 1979 or one with equivalent protection factor) should be used. For inoculations, face shields or visors should be worn.
- 12 Effective disinfectants must be available for immediate use.
- 13 Work surfaces must be disinfected after use.
- 14 All waste materials, including animal bedding, must be rendered non-infective before disposal. Animal carcasses must be incinerated.
- 15 Used animal cages must be rendered non-infective by disinfection, fumigation, heat treatment or autoclaving.
- 16 Materials for autoclaving, or incineration, and used animal cages must be transported without spillage.
- 17 Insect and rodent control measures must be taken.
- 18 All accidents, including animal bites and scratches, must be immediately reported to and recorded by the person responsible for the work.

Animal containment level 3

42 Animal containment level 3 is suitable for work with vertebrates which are deliberately inoculated with organisms in hazard group 3 (or viable material suspected of containing these organisms). Personnel must be experienced in the handling of the animals to be used and a high standard of supervision of the work must be maintained. The person responsible for the animal experiment must ensure that all those having contact with the animals and waste materials are familiar with the local code of practice and are aware of any other precautions and procedures that may be required.

- 1 The animal room must be designed so that it is easily cleaned. Working surfaces, walls and the floor must be impervious to water and should be resistant to acids, alkalis, solvents and disinfectants. Where floor drains are installed e.g. when working with large animals, the drain traps must be kept filled and they must be disinfected and cleaned regularly and at the end of each experiment.
- 2 The animal room must be separated from the general thoroughfare by an anteroom with two doors, or be sited within an animal suite or animal unit. The anteroom must have a wash hand basin fitted with taps which can be operated without being touched by hand, also facilities for storage of protective clothing. Shower facilities must be provided in the anteroom or within the animal suite or animal unit.
- 3 The animal room or suite must be sealable to permit fumigation.
- 4 Access to the anteroom and animal room must be limited to authorised persons. A specific biohazard sign indicating the level of work must be posted at the entry and the animal room must have an observation window. The animal room or suite must be locked when staff are absent.

- 5 A continuous airflow into the animal room must be maintained by extracting air through ducting to the outside air through a HEPA filter, or by extracting air with a fan and HEPA filter sited in a wall or window of the animal room. The ventilation system must incorporate a means of preventing reverse airflows. In facilities which have a mechanical air supply system, the supply and extract airflow must be interlocked to prevent positive pressurisation of the room in the event of failure of the extract fan.
- 6 An autoclave and an incinerator for the sterilisation of waste materials must be available on site. The autoclave should be sited in the same building as the animal room or animal suite, and the incinerator must be readily accessible on site.
- 7 Protective clothing, including footwear and gloves, supplemented where necessary by heavy duty or waterproof clothing, must be worn in the animal room and must be removed when leaving the room. The clothing must be disinfected or autoclaved after use.
- 8 Hands must be washed after removal of protective clothing when leaving the anteroom or animal suite.
- 9 Eating, chewing, drinking, smoking, storing of food for human consumption and applying cosmetics must not take place in the animal room.
- 10 Mouth pipetting must not take place.
- 11 Infective materials taken into the animal room, or removed from it, must be transported in sealed containers.
- 12 All procedures must be performed so as to minimise the production of aerosols. A microbiological safety cabinet should be used (class I or class III, BS 5726: 1979, or unit with equivalent protection factor) for manipulations such as inoculation procedures, necropsy and harvesting of infected tissues and fluids, or alternatively high performance respiratory protective equipment must be worn (see Appendix B). The cabinet must exhaust to the outside air or to the room air extract system.
- 13 Animals infected with group 3 pathogens should be housed in safety cabinets, or isolators, or in partial containment fitments that are provided with HEPA filtered exhaust ventilation, or alternatively, personnel must wear a complete change of clothing and use high performance respiratory protective equipment at all times. Dust producing bedding materials and feedstuff should be avoided.
- 14 Effective disinfectants must be available for immediate use.
- 15 Work surfaces must be disinfected after use and the room disinfected or fumigated at the end of each experiment.
- 16 All waste materials including animal bedding must be rendered non-infective before disposal. Animal carcasses must be incinerated.
- 17 Used animal cages must be rendered non-infective by disinfection, fumigation or heat treatment (steaming or autoclaving). Safety cabinets and isolators must be fumigated after use.
- 18 Materials for autoclaving, or incineration, and used animal cages must be transported without spillage.
- 19 Insect and rodent control measures must be taken.
- 20 All accidents, including animal bites and scratches, must be immediately reported to and recorded by the person responsible for the work who must take the appropriate measures specified in the local code of practice.

Animal containment level 4

- 43 Animal containment level 4 is suitable for work with vertebrates which are

deliberately inoculated with organisms in hazard group 4 (or viable material suspected of containing these organisms). A specific code of practice must be prepared for work at this level and a safety officer (accountable to the person identified as responsible for the work in question) must be appointed. Personnel must be over the age of 18 and must have had specific training in handling animals infected with group 4 pathogens and in the use of the safety equipment and controls of the animal room. The work must be supervised. The person responsible for the animal experiment must ensure that all those in contact with the animals and waste materials are familiar with the local code of practice and are aware of any other precautions and procedures that may be required.

- 1 The animal room and ancillary rooms must be designed so that they can be easily cleaned. Work surfaces, walls, floor and ceiling must be impervious to water and resistant to acids, alkalis, solvents and disinfectants. Where floor drains are installed, the drain traps must be kept filled and the effluent must be rendered non-infective before discharge to a sewage system. The drain traps must regularly be disinfected and cleaned at the end of each experiment.
- 2 The animal and ancillary rooms must be sealable to permit fumigation.
- 3 If the animal room is not an integral part of a containment level 4 laboratory or animal unit, it must form an isolated part of a building. Access must be restricted to authorised personnel and a key procedure established so that the entry is restricted at all times.
- 4 Entry must be through an airlock. The clean side of the airlock must be separated from the restricted side by changing and showering facilities and preferably by interlocking doors. The outer door must be labelled with a 'work in progress' sign.
- 5 The animal room and airlock must be ventilated through independent ducting by a plenum and a total-loss exhaust air system. The exhaust air must be filtered through two HEPA filters mounted in series before it leaves the room. The input air must be filtered through a single HEPA filter. At all times, the airflow must be from the outside area into the room. A negative pressure of 7 mm of water must be maintained in the animal room and a negative pressure of about 3 mm of water in the airlock. An alarm system must be fitted to detect any unacceptable change in air pressure and manometers must be displayed which can be read from both inside and outside the animal room.
- 6 The supply and extract airflow must be interlocked to prevent positive pressurisation of the room in the event of failure of the extract fan and an emergency source of electric supply must be provided to cut in automatically in the event of a power failure. The ventilation system must incorporate a means of preventing reverse airflows.
- 7 An additional ventilated airlock that can be fumigated may be required for passage of supplies, or equipment, which cannot enter through the personnel airlock or autoclave.
- 8 At all times during work in the unit there must be a second authorised person available to assist in the case of an emergency. An observation window, or alternative, must be installed in the working area so that the occupants can be seen.
- 9 Eating, chewing, drinking, smoking, storing of food for human consumption and applying cosmetics must not take place in the animal unit.
- 10 Mouth pipetting must not take place.
- 11 A complete change of clothing must be worn. The clothing must be removed in the dirty side of the changing area after work and placed in a container for autoclaving. A shower must be taken before leaving the unit.

- 12 High performance respiratory protective equipment (two or more units) (see Appendix B), must be available in the clean side of the unit for use in an emergency.
- 13 All effluent, including that from the showers, must be rendered non-infective before discharge to a sewage system.
- 14 A double-ended autoclave with interlocking doors, with entry in the animal room area and exit in a clean area, must be provided. An incinerator must be available on site.
- 15 There must be a telephone, or other means of outside communication, inside the unit.
- 16 All procedures with infective materials should be conducted in a class III microbiological safety cabinet (BS 5726: 1979) or isolator which provides an equivalent level of protection, or alternatively, special protective clothing and high performance respiratory protective equipment must be worn. The exhaust from the cabinet or isolator must pass through two HEPA filters mounted in series before it is ducted to the outside air or to the room air extract system.
- 17 Animals infected with group 4 pathogens must be housed in class III microbiological safety cabinets, or isolators, or in partial containment fitments which are provided with HEPA filtered exhaust ventilation. Where partial containment is used, and in circumstances where containment of the animal is not reasonably practicable, all personnel must wear special protective clothing and high performance respiratory protective equipment at all times.
- 18 Effective disinfectants must be available for immediate use.
- 19 Infective material should be stored in the animal room, but where this is impracticable such material taken into the room (or removed from it to another containment level 4 room on site) must be transported under the supervision of the safety officer, in sealed containers which have been disinfected externally.
- 20 All waste materials must be rendered non-infective before being removed from the animal room and should be autoclaved. Animal bedding materials and carcases must be incinerated immediately on removal.
- 21 A double-ended dunk tank filled with an effective disinfectant may be required for the removal of materials which cannot be autoclaved. Removal of materials in this manner, also material removal through the equipment airlock, must be undertaken only with the authorisation of the safety officer and under conditions defined in the local code of practice. The dunk tank should be sealed during fumigation if the disinfectant is incompatible with the fumigant.
- 22 Insect and rodent control measures must be taken.
- 23 When animals are not totally contained within a class III microbiological safety cabinet (BS 5726: 1979 or one with equivalent performance) only one pathogen should be in use in the animal room at one time and the safety officer must ensure that all disinfection or fumigation procedures are effective.
- 24 All accidents, animal bites and scratches and accidental exposure to infective materials must be immediately reported to and recorded by the safety officer who must take the appropriate measures specified in the local code of practice.

Appendix A

The use of class II microbiological safety cabinets

- 1 References should be made to BS 5726: 1979 '*Specification for Microbiological Safety Cabinets*', British Standards Institution, London for a full description of the three types of safety cabinet, class I, II and III, also the methods for testing air velocity, filtration efficiency and for determining the level of protection provided by these cabinets (the 'operator protection factor').
- 2 The class II cabinet is designed to control airborne contamination of the work while at the same time reducing the exposure of the operator to airborne particles which are dispersed inside the cabinet during the work procedures. In the simplified form of cabinet these two functions are achieved by a recirculating downward flow of filtered air over the work area; part of this airflow is exhausted to the atmosphere through a HEPA filter and make-up air is drawn into the cabinet through the open work front.
- 3 The inward airflow that is drawn through the working aperture of open-front cabinets (class I and II) can be disturbed by, for example, sudden movements of the arms of the operator and turbulence around the equipment placed inside the cabinet, persons moving across the front of the cabinet and by air movements in the room or changes in air pressure. Disturbances of this kind may affect the level of protection for the operator particularly when a class II cabinet is used since this type generally has a lower inward air velocity through the upper areas of the work front than a class I cabinet. For this reason, class II cabinets are not recommended for work with group 3 pathogens and must not be used for group 4 pathogens.
- 4 Before a class II cabinet is selected, the user should assess the need for protection of the work and relate this to the operator protection factor that can be achieved in the prevailing conditions of use. The cabinet must be correctly sited and should be used only by appropriately trained personnel. Careful working procedures will be essential and access to the laboratory should be restricted whilst the cabinet is in operation.
- 5 In certain conditions some class II cabinets will provide a protection factor of the same order as class I cabinets (i.e. a factor of 10^5 or better, BS 5726: 1979). If it can be shown by in-use tests that this level is achieved consistently (as demonstrated by tests carried out at regular intervals, the frequency of which will depend on use) and provided that the local safety management will allow, a class II cabinet may be used for some work with group 3 pathogens where protection of the work is essential. Consideration should always be given however to the use of a class III cabinet which will provide a high level of protection for both the work and the operator.
- 6 Advice on technical matters and supply of microbiological safety cabinets can be obtained from DHSS, Scientific and Technical Branch, 14 Russell Square, London WC1B 5EP; on installation from DHSS, Works Group, Euston Tower, 286 Euston Road, London NW1 3DN; or from appropriate offices of the Scottish Home and Health Department, the Welsh Office and the Department of Health and Social Services, Northern Ireland.

Appendix B

Respiratory protective equipment

- 1 Where respiratory protective equipment is used in situations of microbiological hazard, the person responsible for the work must ensure that the equipment used affords adequate protection for the risks involved.
- 2 The standard of protection obtained by the use, for example, of a class I microbiological safety cabinet is a filter penetration less than 0.003% with an overall protection factor of 10^5 . In general, and to be consistent with this standard, a minimum protection factor of 10^5 will be required of respiratory protective equipment where significant aerosols may be created. This standard is only likely to be achieved by high performance respiratory protective equipment.
- 3 Users should therefore ensure, in conjunction with manufacturers and suppliers, that the respiratory protective equipment to be used is designed and maintained to meet this standard of protection.
- 4 There is at present no **approved** respiratory protective equipment for work involving microbiological risk,* but there is a legal requirement for such approved equipment used in certain other industries and processes. Certificates of approval are issued by HSE and inspectors refer to these when recommending respiratory protective equipment for use in appropriate situations. The approved list is also used for reference purposes when considering respiratory protection in situations where approval is not a legal requirement.

* i.e. approved pursuant to certain regulations made under the Health and Safety at Work etc Act 1974 and the Factories Act 1961 and listed in the current HSE Certificates of Approval (Respiratory Protective Equipment) 1981: Form 2486, obtainable from HMSO.

Appendix C

Containment of latently infected animals*

1 It is recognised that animals can harbour infectious agents which are acquired naturally. Some of these infections, lymphocytic choriomeningitis and *Herpesvirus simiae* (B virus) for example, can give rise to a chronic carrier state or the agent might persist in a latent non-infective form which can be reactivated periodically or as a result of certain stimuli. Although the risk to handlers from such agents may be slight, management systems and facilities should be reviewed before handling animals likely to harbour latent zoonotic agents.

2 The predisposition of certain species of monkey (e.g. rhesus and cynomolgus types) to carry B virus in a latent state is of particular concern because although the risk of acquiring infection from monkeys may be small the consequences of infection are serious: more than 85% of the reported cases have proved fatal and survivors are likely to be left with residual neurological damage.

3 The B virus antibody status of monkeys used in experiments must be known. Wherever possible only those animals that are free from B virus should be used. They may come either from colonies free from B virus or from selected monkeys that have been kept isolated and found to be B virus antibody negative on two occasions separated by two months. Seronegative monkeys should be kept separated from seropositive monkeys, preferably in a separate room.

4 If monkeys with B virus antibodies are used experimentally, there is a risk of transmission of the virus to man either by bite or by exposure to monkey tissues and appropriate measures must be taken:

- (a) to prevent monkey bites occurring;
- (b) to wear appropriate protective clothing including gowns and gloves;
- (c) to draw up a code of practice which must include the procedures to be followed in the event of a bite; and
- (d) to provide a containment level not less than animal containment level 2.

5 Experiments involving surgery of the oropharyngeal region of the dorsal and cerebral ganglia and of the vaginal area should be carried out only in B virus negative monkeys.

6 When monkeys or other vertebrates are experimentally inoculated with B virus, or experiments are undertaken to reactivate the virus, a level of containment not less than animal containment level 3 with appropriate procedures for medical surveillance and treatment must be used.

Latency of B virus in monkeys†

7 B virus, as its latinized name of *Herpesvirus simiae* implies, is a simian counterpart of the human herpes simplex virus (*Herpesvirus hominis*). The natural history of B virus in its simian hosts, various species of asiatic macaques, would thus be expected to resemble the natural history of herpes simplex virus in man. The latter is characterised by life-long latent infection following primary infection. Periodic shedding of virus occurs, both spontaneously and after exposure to certain, usually stressful, stimuli: such shedding appears to occur several times during a year and is not necessarily associated with visible herpetic lesions. Two major sites of viral excretion are recognised in man: the oral cavity and the genital tract; these two sites correspond to the major portals of entry of the virus and are linked with proven latency of the virus in the ganglia of sensory nerves subserving these two portals of entry.

8 Work carried out at Porton by the MRC-supported B virus unit has shown that, although the natural history of B virus in monkeys does show some similarities with that of herpes simplex virus in man, there are also distinct differences. The similarities include the establishment of latent infections in the

* See also: A statement by the MRC Simian Virus Committee: The Management of Simians, July 1978.

† (E A Boulter).

ganglia of sensory nerves, both in the trigeminal nerves subserving the oral cavity, and in the sacral ganglia subserving the genital tract. One major difference is that B virus can only be recovered from these ganglia in about 50% of seropositive monkeys, compared to a recovery rate of almost 100% of seropositive human individuals. Two alternative explanations of this discrepancy are that either only 50% of seropositive monkeys are latently infected or that latent B virus is more fully integrated into its host cell and thus less easily re-activated to its infectious form. Consideration of data discussed below would suggest that the latter is the more likely explanation.

9 Work extending over several years has revealed a further distinction between the natural histories of the simian and human infections. Despite long periods of intensive sampling, no periodic spontaneous excretion of B virus by singly-caged seropositive monkeys has been detected. Furthermore, numerous attempts to induce re-activation, using methods known to be effective with other herpes viruses in both man and experimentally infected animals, have, with one exception, failed. The single exception was one of six female monkeys given a course of treatment with the immunosuppressive agent, antilymphocyte globulin. This particular monkey excreted B virus for several days in its vagina and, on one occasion, from its mouth. The only conclusions that can be drawn from these observations is that either B virus in monkeys is less readily re-activated than herpes simplex virus in man or that it is re-activated by stimuli other than those effective on the latter virus or, more probably, that both of these conclusions are true.

10 Further light has been shed on the natural history of this simian herpes virus by the study of seroconversions in breeding colonies. Several such episodes have been observed among the breeding colonies at Porton. In each instance, the setting up of a new colony consisting of seronegative monkeys, but including one monkey with a very low titre of neutralising antibody, has resulted in all the animals developing high titres of neutralising antibodies within a period of up to eight weeks. In all but one of these instances, examination and swabbing of the entire colony failed to reveal either clinically evident infection or the presence of infectious virus in body secretions. The one exception related to an epizootic in a recently established colony where only a fraction of the colony had seroconverted at the time of the initial serological screen. In this instance virus was recovered from a vaginal swab taken from a monkey with no clinical signs of infection. Within the next ten days, the remainder of the colony had become seropositive. Despite this rapid transfer of infection within colonies, there has been no spread from an infected colony to adjacent colonies on either side, even though the wide-mesh screens between the colonies allowed some contact between their inhabitants to occur. Furthermore, no spread of infection between singly-caged animals, in which tactile contact was frequently seen, has been noted; neither did four seropositive pregnant females, taken from an epizootic in a breeding colony succeed in passing their infection on to their young, either at birth or during the subsequent year in which parent and offspring were caged together. It would appear that some factor, or factors, that occur within a breeding colony favours re-activation of latent B virus in monkeys, and that spread of infection to all the inmates then occurs rapidly. The nature of this factor, or factors, and the mode of spread of infection, remain unidentified but a reasonable assumption is that sexual activity plays a large part in both. Close physical contact appears to be essential for transfer of infection, but the failure of mothers to infect their offspring in the same cage indicates that certain other conditions need to be present before physical contact results in cross-infection. All the evidence suggests that aerosol spread of infection does not occur.

11 In summary, B virus does produce latent infection in its natural host but this latent infection rarely gives rise to excretion of infectious virus. Certain, so far unidentified, conditions present in newly established breeding colonies do predispose to both re-activation and transfer of infection from monkey to

monkey but, once this epizootic has ceased, excretion of virus once more becomes a very rare event. No evidence of aerosol, or other forms of non-contact spread, has ever been noted. Spread of infection from monkey to man, from published case histories, appears also to require close contact between monkey and man.

Appendix D Invertebrates

1 The important invertebrates are:

Protozoa
Platyhelminthes
Aschelminthes
Mollusca
Annelida
Arthropoda
Echinodermata

2 These may contain or might be used for work with organisms in each of the four hazard groups or with viable materials suspected of containing them.*

3 The containment levels listed for animal rooms (paras 37 to 43) apply in principle for invertebrates but in addition, the following general comments must be borne in mind:

- (a) separate rooms must be used for infected and uninfected invertebrates;
- (b) invertebrates can be allocated according to whether they;
 - (i) live in water (aquatic);
 - (ii) are amphibious;
 - (iii) crawl or jump;
 - (iv) fly;
- (c) aquatic or amphibious invertebrates must be kept in tanks with lids to prevent escape;
- (d) for invertebrates that crawl, jump or fly, the following further precautions are necessary;
 - (i) entry to the rooms must be through an airlock. Consideration should be given to the use of 'insectocutors' in the airlock;
 - (ii) rooms must be insect proof and a large laboratory sink should be provided with adequate traps for waste. Waste should always be treated before disposal, preferably by heat. Measures should be taken to enable escaped invertebrates to be easily detected and recaptured or destroyed. Use of insecticidal sprays might be necessary in an emergency at very high levels of risk but it should be remembered that the use of insecticides in a small room may render the room unfit for handling invertebrates for a long period, if not permanently. For ticks and mites, containers should be kept over trays of oil;
 - (iii) ventilation must be screened;
 - (iv) waste should preferably be treated by heat, as waste may harbour invertebrates which may not be killed by disinfectants;
 - (v) all experimental cages/pens must be numbered and documented;
 - (vi) at containment levels 1 and 2, flying or crawling arthropods should be handled on white trays to detect escape;
 - (vii) at containment levels 3 and 4, flying or crawling arthropods must be counted into small containers and be accounted for. They should also be handled in safety cabinets, isolators or partial containment fitments that are provided with HEPA filtered exhaust ventilation;
 - (viii) flying insects infected with group 3 pathogens should be kept in double netting cages;
 - (ix) the activity of the arthropod and the risk of accidental escape can be reduced by chilling.

* Invertebrates can also harbour infectious organisms e.g. borrelia in soft ticks, trypanosomes in triatomid bugs, organisms from sewage in mollusca, crustacea or echinoderms. Such invertebrates should be kept at a containment level appropriate to the risk.

Appendix E[§]

Recommendations on physical containment requirements for work on specimens from patients who may be infected with group 4 pathogens or rabies virus

Introduction

Group 4 pathogens include viruses which cause encephalitis and viral haemorrhagic fevers. These will present clinical and laboratory problems in the UK and laboratory containment requirements are therefore dealt with in detail in this appendix. Rabies virus although a group 3 pathogen presents problems both in the laboratory and in the management of human cases and is included here. As smallpox has been eradicated and no stocks of group 4 poxviruses are held in the UK these will not be considered further.

In carrying out the recommendations below in the context of formulating written local codes of practice, laboratories will in the case of most group 4 pathogens and rabies (group 3) need to have regard to the requirements of the Health and Safety (Dangerous Pathogens) Regulations 1981 (SI 1981/1011).^{*} These Regulations state, *inter alia*, that an employer or self-employed person shall not carry out a diagnostic service in relation to a 'listed pathogen'[†] unless at least 30 days in advance he has notified HSE of certain particulars set out in Schedule 3 to the Regulations. In this context 'diagnostic service' means any activity carried on with the intention of:

- (a) identifying a listed pathogen;
- (b) isolating or identifying other organisms from specimens or samples suspected of containing a listed pathogen;
- (c) analysing specimens or samples from a patient known to be, or suspected of harbouring a listed pathogen for purposes relating to the assessment of the physical progress or assistance in the clinical management of that patient.

The requirement to notify diagnostic work does not extend to cases where the listed pathogen is known or suspected to be in a human or animal body (the effect of this is to exclude work which occurs in the context of clinical treatment or post-mortem analysis, although work on a specimen or sample taken in the course of such treatment or analysis is not excluded). It is limited to the initial provision of particulars specified in Schedule 3 of the Regulations and does not apply to each **separate** piece of work.

Viral haemorrhagic fevers

These guidelines are based on the concept that there are urgent bacteriological, parasitological and possibly other clinical pathological procedures, **none of which involve or allow the replication of virus**, which may need to be carried out on patients when the level of suspicion of a viral haemorrhagic fever is low, or in the period before a patient with suspected infection could be transferred to a high security isolation unit. They are intended to aid in the formulation of written local codes of practice which should be agreed between clinicians and the laboratory concerned.

The object of the examinations is to preserve life by identifying treatable conditions which may be the cause of the patient's illness and there is no intention that the definition of laboratory facilities for these emergency procedures should lead to the concept that transfer of patients to a high security isolation unit should, in any way, be delayed where infection with a group 4 pathogen is a strong possibility.

Clinicians should consider the possibility of a viral haemorrhagic fever in any person developing a febrile illness within 21 days of arrival from an endemic area (e.g. tropical Africa) or in any laboratory worker in a containment level 4 laboratory or animal house presenting with an unexplained fever.

[§] It is intended that this Appendix will be reproduced in a memorandum on viral haemorrhagic fevers being produced by the DHSS.

^{*} See *A guide to the Health and Safety (Dangerous Pathogens) Regulations 1981* Health and Safety series booklet HS(R)12, published by HMSO. (ISBN 0 11 883454 1).

[†] See footnote page 10 ACDP Report.

The problem must be discussed with the diagnostic laboratory and the appropriate containment level for laboratory investigations established before any specimens are sent (see Fig 1). Such specimens must be clearly marked with a special label used only for this purpose and should be despatched as agreed between the clinician and the laboratory whose advice should be in accordance with the recommendations on the transport of specimens set out in *The Code of Practice for the Prevention of Infection in Clinical Laboratories and Post-mortem Rooms*. The laboratory request form must indicate the level of suspicion of a group 4 infection and be signed by a consultant or a deputy designated by the consultant.

Although any cause of fever must be considered in a febrile patient suspected of group 4 infection the main life-threatening but treatable microbial diseases to be considered are, for instance, malaria, typhus, typhoid fever or other septicaemic illness. In unconscious patients relevant investigations may well include those for the diagnosis of diabetes. The infection requiring the most rapid action is malaria and an exclusion test should be done as soon as possible. Although additional blood samples and other specimens may be taken at the same time no work must be done on them before the result of the malaria film examination is known and an assessment as to the standard of laboratory facilities required has been made (see Fig 1).

Specimens from patients where viral haemorrhagic fever (VHF) due to infection with a group 4 pathogen is a clinical possibility.

The laboratory containment facilities described below are graded depending on the degree of suspicion of infection based on clinical and epidemiological factors and on the result of the examination of the malaria film. Patients will either:

- (a) have developed a fever having returned from Africa or other countries where such infections are known to occur within a time span of less than an incubation period of three weeks; or
- (b) have had contact with such patients or group 4 viruses in the course of medical care or laboratory work, or by intimate association.

An approach to the problem of patients in (a) above is described by Emond, Smith and Welsby (1978: Brit Med J 1, 966-7) and a similar approach for the classification of specimens has been adopted in this appendix. There must always be close consultation between the clinician and the laboratory before **any** laboratory investigation is undertaken and in patients returning from abroad the only infection to be excluded as a matter of urgency will be malaria.

Minimal risk

- 1 These are patients who have come from cities where the risk of VHF is negligible. It is reasonable also to include in this group patients who, although they may have visited small towns or country districts, have been diagnosed on clinical grounds as having malaria and confirmation of this diagnosis is sought.
- 2 **No laboratory work must be carried out on specimens from these patients until a blood film has been examined for the presence of malarial parasites**
- 3 The blood film should preferably be prepared and rendered safe at the bedside. (see para 4). If blood is sent to the laboratory for this purpose a class I microbiological safety cabinet (BS 5726 or one with equivalent protection factor) must be used.
- 4 Air-dried thick films should be fixed in 10% buffered formalin* for 15 minutes. Thin films should be fixed initially in methanol for 5 minutes and

* 10% buffered formalin pH 7.2.
 Formaldehyde solution (37/40% W/V) 500 ml
 Sodium dihydrogen phosphate ($\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$) 22.75g
 Disodium hydrogen phosphate (Na_2HPO_4) 32.5g
 Dist H_2O 4 500 ml

then in formalin as for thick films. After formalin treatment, films should be washed in buffered water at pH 7.0 three times and then stained. Alternatively thin films may be rendered safe by fixing in methanol for 30 minutes followed by dry heat at 95°C for 1 hour. Blood films which have been rendered safe can be handled without restriction.

- 5 Reagents, containers and associated equipment used to prepare slides or transport blood should be autoclaved before disposal.
- 6 Normally the demonstration of malarial parasites will establish the diagnosis and specimens may then be handled in routine clinical laboratories, but it should be remembered that malarial parasites may be present in patients with other diseases.
- 7 If malarial parasites are not demonstrated the categorisation of the patient must be reassessed (see Fig 1) and if infection by a group 4 pathogen is still a possibility specimens must be handled in a containment level 3 laboratory using a class III microbiological safety cabinet (BS 5726) or a class III/I microbiological safety cabinet in the class III mode. If viral haemorrhagic fever as a diagnosis is discarded after reassessment by clinical and laboratory staff, specimens may be handled in routine clinical laboratories.

Moderate risk

- 8 Infection with a group 4 pathogen is on epidemiological grounds a distinct possibility, e.g. the patient has stayed or worked in small towns or country districts but the more likely clinical diagnosis is malaria and laboratory confirmation is required.
- 9 **No laboratory work must be carried out on specimens from these patients until a blood film has been examined for the presence of malarial parasites**
- 10 The blood film should preferably be prepared and rendered safe at the bedside (see para 4). If blood is sent to the laboratory for this purpose it must be a containment level 3 laboratory and a class I (BS 5726) microbiological safety cabinet must be used.
- 11 If malarial parasites are demonstrated and viral haemorrhagic fever as a diagnosis is discarded after reassessment by clinical and laboratory staff specimens may be handled in routine clinical laboratories.
- 12 If, after reassessment by clinical and laboratory staff, the possibility of a group 4 infection can not be excluded, whether or not malarial parasites have been demonstrated, specimens must be handled in a containment level 3 laboratory in a class III (BS 5726) microbiological safety cabinet or a class III/I microbiological safety cabinet in the class III mode (see para 19).

High risk

- 13 Infection with a group 4 pathogen suspected e.g. the patient has been living and working in an endemic rural area; is in particular a medical, nursing or ancillary worker from a hospital in an endemic area; has had intimate association with a patient suffering with a group 4 infection; or works in a laboratory where group 4 pathogens are in use.
- 14 **No laboratory work must be carried out on specimens from those patients coming from malaria endemic areas until a blood film has been examined for the presence of malarial parasites.** If the patient has worked in a laboratory where group 4 pathogens are in use the expectation is that the patient would be transferred immediately to a high security isolation unit.
- 15 The blood film should preferably be prepared and rendered safe at the bedside (see para 4). If blood is sent to the laboratory for this purpose it must be a containment level 3 laboratory and a class III (BS 5726) microbiological safety cabinet or a class III/I microbiological safety cabinet in the class III mode must be used.

- 16 If malaria parasites are demonstrated and viral haemorrhagic fever as a diagnosis is discarded after reassessment by clinical and laboratory staff specimens may be handled in routine clinical laboratories.
- 17 If malaria parasites are demonstrated but infection by a group 4 pathogen is still a probability or if malaria parasites are not demonstrated, specimens for non-virological work which is essential before the patient is transferred to a specially designated high security isolation unit must be handled in a containment level 3 laboratory in a class III (BS 5726) or class III/I microbiological safety cabinet in the class III mode.
- 18 Specimens for group 4 virus serology or isolation must be sent to the Special Pathogens Reference Laboratory, CAMR, Porton, which must be forewarned that the specimen is being sent for examination. CAMR will give guidance on the packing and transport of specimens. Specimens for the diagnosis of other viral infections may be sent to other laboratories which comply with the requirements for containment level 4, but only with their consent.

Laboratory procedures

- 19 When there is a likelihood of many hours delay before a patient is transferred to a unit designated for the management of viral haemorrhagic fevers, specimens such as blood for culture and other tests may be taken at the same time as blood for malaria examination so that these specimens or results may accompany the patient to the high security isolation unit. If for example a blood culture is incubated to enable early diagnosis of a septicaemic illness, e.g. typhoid, or patient management tests are required, all work on these specimens must be carried out in a containment level 3 laboratory in a class III microbiological safety cabinet.
- 20 Potentially infectious material to be removed from a class III safety cabinet for incubation, or storage must first be placed in hermetically sealable containers which are disinfected by immersion in, or wiping down with, fresh 2% glutaraldehyde before removal (strong hypochlorite containing 2 500 ppm available chlorine is suitable for this purpose but may damage some metals). Such hermetically sealed containers must not be reopened unless they have been transferred back into a class III microbiological safety cabinet. Sealed units must be used for centrifugation and they must be opened only in a class III microbiological safety cabinet.
- 21 Material for transport to a containment level 4 laboratory must be packed according to instruction given by the receiving laboratory.
- 22 All waste materials and discarded clothing must be rendered safe to handle before they are removed from the laboratory and autoclaved before disposal or recycling.
- 23 Water used for hand washing must be rendered safe by either chemical or heat disinfection.
- 24 When a patient has been transferred to a high security isolation unit, specimens for group 4 virus serology or isolation would be dealt with as in **para 18**. Clinical management tests with specimens from patients with proven group 4 infections must be undertaken in a laboratory which complies with the requirements for containment level 4 with the exception that there need be only single HEPA filtration of exhaust air from the laboratory (as opposed to double HEPA filtration of such air when viral replication is undertaken). A suitably installed flexible film isolator within a high security isolation unit may be used for this work and in these circumstances specific arrangements must be made for the safe disposal of solid and liquid waste.

Viral encephalitis due to group 4 pathogens

- 25 Some group 4 pathogens cause encephalitis (e.g. Russian spring – summer encephalitis) and may arise in a patient or laboratory worker. Specimens for virus diagnosis should be dealt with as in para 18. Specimens for other clinical pathological examinations should be handled in a containment level 3 laboratory in a class III (BS 5726) microbiological safety cabinet or a class III/1 microbiological safety cabinet in the class III mode.

Facilities required where a patient is suspected of having or is proven to have rabies (see Fig 2)

- 26 There is no evidence that blood from patients with clinical rabies contains rabies virus. Virus may, however, be present in saliva, tears, urine, CSF and tracheal aspirates for at least two weeks after the onset of symptoms.
- 27 When biochemical or haematological investigations on blood specimens only are required the work may be undertaken in a laboratory which complies with the requirements of work at containment level 2.
- 28 When non-virological investigations on any specimens other than blood are required, the work must be undertaken in a containment level 3 laboratory and a class I microbiological safety cabinet should be used. Staff performing this work must be vaccinated against rabies. Gloves should be worn for all manipulations which should be undertaken with care and where possible, without the use of needles or glassware, to avoid the possibility of skin puncture. Manual techniques are preferable but if automated equipment must be used it should be disinfected after use by washing through with an effective disinfectant compatible with the system. Where there is no compatible disinfectant distilled water or the manufacturer's wash fluid should be run through to dilute any residual virus. Waste from this rinsing process must be rendered safe before disposal.
- 29 Specimens for virological and antibody testing should be sent to the Virus Reference Laboratory, Central Public Health Laboratory, Colindale Avenue, London NW9 5HT which should be forewarned and will advise on a safe means of packaging and transportation.

Fig 1 Handling of specimens from patients who may be infected with a group 4 pathogen. Risk assessment and laboratory facilities.

No laboratory work must be carried out on specimens from these patients until a blood film has been examined for the presence of malarial parasites

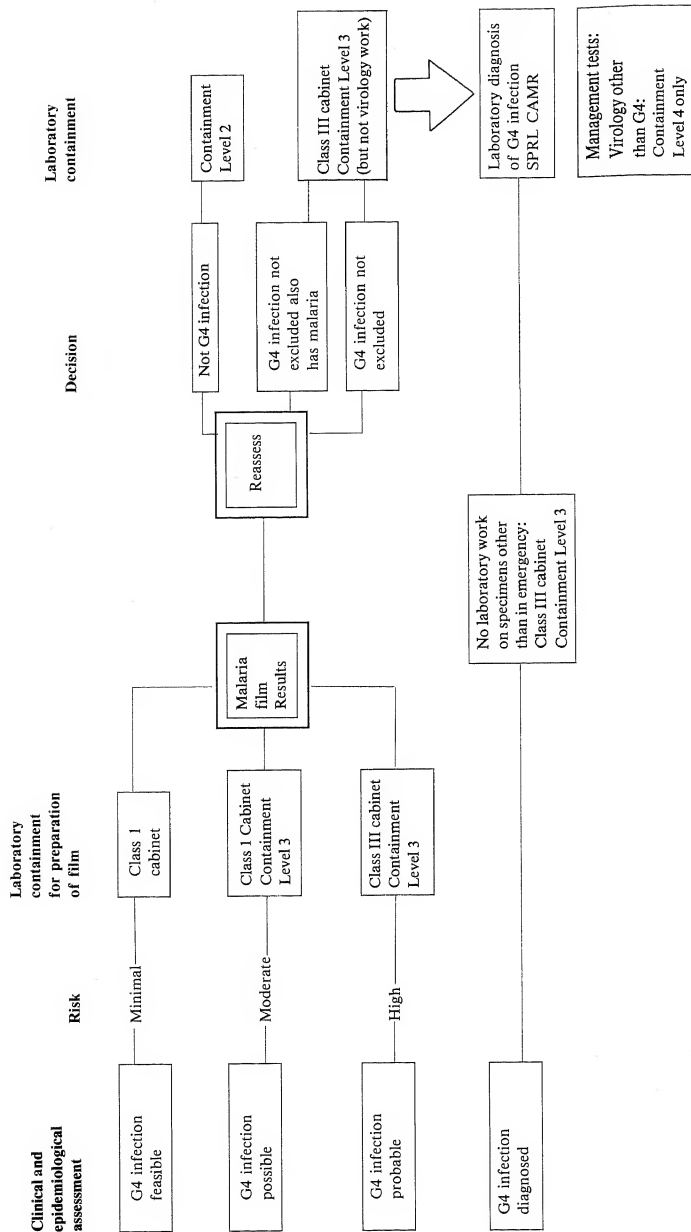
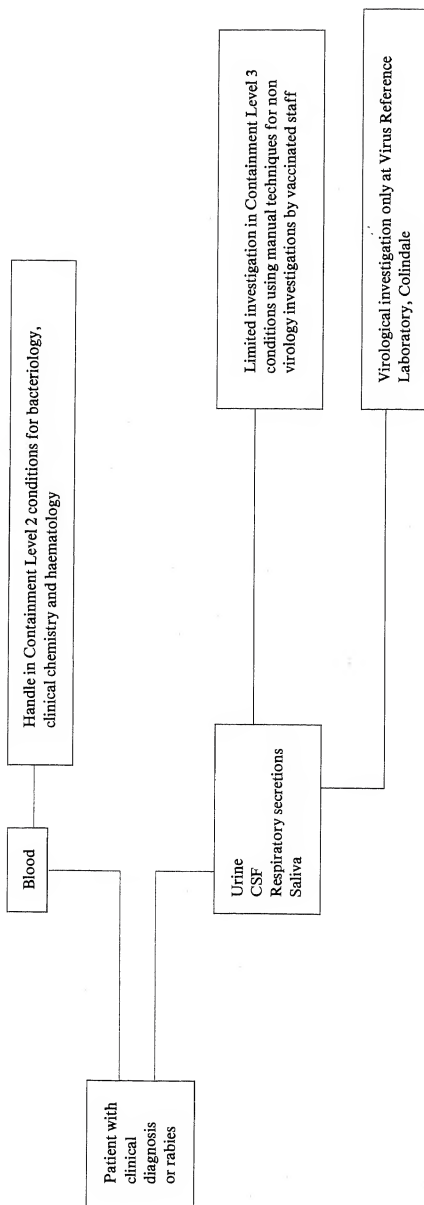


Fig 2 Facilities required where a patient is suspected of having or is proven to have rabies.



Appendix F

Containment facilities in high security isolation units

- 1 In January 1975, DHSS asked regional health authorities to make emergency arrangements to designate a number of the existing infectious disease units for the reception of Lassa fever cases and suspects. They were each asked to choose and nominate a suitable infectious disease unit and a list of these was published in 1976 in the 'Memorandum on Lassa Fever'.
- 2 Following the designation by regions of these units, the workload turned out to be much less than expected. A number of designated units did not admit either a proven or suspect case. In addition, staff were sometimes reluctant to volunteer for work in them and the finance to update and upgrade their facilities was hard to find. Five of the units did, however, develop their techniques and equipment and informally agreed their catchment areas. These units have developed different procedures because of their differing ideas, geography, manpower and finances.
- 3 We understand it is now the intention of the DHSS to formally designate a number of these units for this work. We believe that before this is done there should be an agreed code of practice specifying the requirements for the containment and prevention of spread of organisms by air-borne and other routes, for the protection of both the staff and the public, and that the code should be reasonably consistent with that to be used in laboratories.
- 4 We have been informed that the Health Ministers have set up a working party to review the 'Memorandum on Lassa Fever' and its accompanying notes and we welcome this action.
- 5 Whilst accepting that the nature of the isolation required by any individual patient or disease remains at the clinician's discretion, we hope that the working party will clarify the relation of risks to the type and stage of the diseases they discuss and review the requirements for physical containment of the patient. We think it is particularly important that they take note of ACDP's views (see Appendix E) on procedures to be adopted at the 'interface' between clinical care and laboratory work, and also that they review the procedures relating to communication with the laboratory, the transport of specimens, disinfection policy and the conduct of post-mortem examinations.

Appendix G

Containment requirements for work with rabies virus materials

The risk to laboratory workers

1 We have been asked particularly to comment on the hazard classification of rabies virus. This is a highly pathogenic virus for which there is no treatment once the symptoms of disease have begun. Infection is usually through the skin or less commonly the mucous membranes. Prophylactic vaccination is effective and in recent years has become very reproducible, simple and harmless; we therefore believe that only vaccinated subjects must be allowed to handle the virus.

2 For diagnostic and laboratory work where it is not intended to propagate the virus, containment level 3 is considered to be adequate for the human risk. However, for work requiring the propagation of rabies virus, secondary containment to a level comparable with the standard required at containment level 4 becomes essential because of the increased potential risk of an escape of the virus to the animal population.

The risk to animals

3 Britain is rabies free, there having been only two cases of the disease in animals (in 1969 and 1970 in two imported dogs) since 1922. MAFF has the responsibility of ensuring that rabies does not gain entry to the animal population of Britain. If the disease did enter Britain and become established in our domestic and wild animal populations, the effects would be disastrous to animal (and human) health and would inevitably alter our whole approach to human contact with pets and other animals.

4 In relation to laboratory work with rabies virus, the prime concern of MAFF is to ensure that there can never be any accidental escape of rabies virus from any laboratory into the native animal population. In exercise of the powers granted to MAFF by the Rabies Virus Order 1979, MAFF requires that the **secondary containment** of any laboratory working with the virus must be of the highest level, comparable with the standards recommended by ACDP for work with pathogens in hazard group 4 (see paras 35, 36 and 43).

Appendix H

Hepatitis B virus

1 We were asked particularly to examine the problems of the classification of hepatitis B virus. A number of our members had expert knowledge of the subject, but we are also indebted to ASTMS and the Joint Working Party* for permission to use documents they prepared in order to produce the following summary of knowledge of the incidence of infection and disease and the possible modes of transmission.

2 Hepatitis B virus is one of the most frequent causes of infection in the world as a whole. It is common and widespread in the tropics but also occurs regularly in the UK, though much less frequently. It is particularly common in certain sub-groups of the population, e.g. drug abusers or practising male homosexuals. Approximately 0.1% of the population are carriers and are clinically well, but infection is associated with acute and recurrent hepatitis and cirrhosis and, in certain areas of the world, with hepatocellular carcinoma. However, in the UK in general it is a minor cause of hepatitis which usually resolves without incident and even post-transfusion hepatitis is now due more often to the non-A non-B agents than to hepatitis B virus.

Sources of hepatitis B virus

3 Almost all body secretions and excretions that have been examined from either an acute case of infection or a carrier of hepatitis B virus have been shown in at least some cases to contain HBsAg, including blood, urine, saliva, sweat, tears, breast milk, synovial fluid and semen.¹ However the presence of HBsAg does not indicate the presence of complete, infectious virus. Faeces are not considered to be infectious, and so far only blood (serum/plasma), concentrated saliva and concentrated semen have produced infection when inoculated into chimpanzees.^{2,3} Of all the potential sources of infection, blood is the most common.

Routes of transmission

4 In the laboratory there are three relevant routes of transmission:

- (a) percutaneous transmission by needle or other sharp object, e.g. accidental needle prick, accidental stab with broken pipette;
- (b) percutaneous transmission by contamination of cuts, scratches, abrasions, burns etc;
- (c) contamination of mucosal surfaces of mouth, nose or eyes. Direct transmission is possible by mouth pipetting or from splashes. Direct contact with a contaminated surface and then from hand-to-mouth, or hand-to-eye is obviously less likely but recent studies⁴ have demonstrated that HBsAg can be detected on the surfaces of specimen containers, equipment and benches in clinical laboratories.

5 With many viruses the most common route of infection is by aerosol spread. There is no evidence that hepatitis B transmission occurs naturally by this process. Attempts to produce infection in chimpanzees by spraying concentrated infectious saliva into the mouth were unsuccessful, although the same material produced infection when inoculated percutaneously.⁵ In a haemodialysis centre serving a population with a high percentage of HBsAg positive patients, HBsAg was not detected in aerosol samples taken from the treatment area, from the laboratory area while specimens were processed, or from the area where re-usable dialysers were disassembled and cleaned.⁶ In addition, air samples from a dental surgery taken during treatment of HBsAg positive patients whilst using procedures known to favour aerosol formation, were totally negative for HBsAg.⁷ The production of a true aerosol, i.e. particles less than 10µm in diameter, from blood or serum is difficult, a fact also noted by the MRC Working Party investigating transmission of infection in haemodialysis units.⁸

* Joint Working Party on the Prevention of Infection in Clinical Laboratories of the Association of Clinical Biochemists, Association of Clinical Pathologists, Institute of Medical Laboratory Sciences, and the Royal College of Pathologists.

6 Some laboratory manipulations, although not producing true aerosols which can infect by inhalation at some distance from the operator, do produce droplets which are a hazard to the operator. Large droplet transfer into the eyes, mouth or onto cuts and broken skin may transmit infection. In any technique where splashing is a possibility, precautions should be taken to avoid contamination of mouth, eyes or hands. Such droplets can also contaminate surfaces and equipment etc from which infection may be acquired by contact.

Hazard to laboratory workers

7 Laboratory workers process blood, blood components and blood-contaminated fluids and secretions; those taken from patients with hepatitis B virus are effective vehicles of transmission of infection. Therefore laboratory workers and all other personnel dealing with blood must be at greater risk of exposure to hepatitis B virus than the general population.

8 Hepatitis B infection does occur in laboratory staff. The continuing survey by the Association of Clinical Pathologists^{9,10} and the report of Harrington and Shannon¹¹ document such cases. However, it is important to note that the figures of Harrington and Shannon were for 1971 and 1973, and those of the Association show an apparent decline in attack rate since 1975 (Table 1). In addition, the Harrington and Shannon data were for hepatitis due to all causes, not solely hepatitis B virus.

9 Although the number of cases per year has remained almost static since 1975, the number of staff employed and especially the number of clinical specimens processed has increased. Polakoff¹² has published figures for hepatitis B infection in laboratory staff in England, Wales and Northern Ireland from 1972 (Tables 2 and 2A). These are taken from returns of all hepatitis B infections sent to the Communicable Disease Surveillance Centre, Colindale; they cover a more extensive population and can be considered reliable especially after 1975 when hepatitis B virus infection was legally defined as an industrial disease. It should be noted that these independently acquired data also show an apparent fall from 1975 onwards in the number of laboratory personnel affected. Cases of infection in laboratory staff in Scotland taken from returns to the Communicable Diseases Scotland Unit have been added in Table 3 to give more comprehensive data.

10 The statistics on hepatitis B infection in laboratory workers may be incomplete and there is little information available on other occupational groups such as for example prison officers. Some cases in laboratory workers might have been acquired socially, but it appears from the figures that certain groups of laboratory workers have a higher attack rate for hepatitis B than the general public and than others working in hospitals such as nurses.

11 Much of the concern surrounding hepatitis results from the severe outbreaks of hepatitis in the Manchester and Edinburgh renal units some ten years ago,^{13,14} but these two outbreaks may have been atypical (Table 4). Recent data on the Edinburgh outbreak suggests that hepatitis B infection was present in the unit before the outbreak without producing fatalities and that the severity of the outbreak could be attributed to a double infection with hepatitis B virus and another hepatotoxic agent.¹⁵ Immediately after the Edinburgh outbreak a programme of regular screening of staff and patients in renal units was introduced throughout the United Kingdom. This has proved to be an effective control measure.

12 Not all specimens that are HBsAg positive present an equal risk of infection to laboratory staff. Present evidence indicates that specimens which are HBsAg positive and contain antibody to HBeAg are much less infectious than those which are HBsAg and HBeAg positive.¹⁶ Specimens that contain HBsAg but neither HBeAg or anti HBe should be considered as though they were potentially infectious. Data from blood transfusion services in England and Scotland^{17,18} indicate that under 20% of HBsAg carriers are also HBeAg positive although among some ethnic minorities e.g. Chinese, Vietnamese, up to 50% of HBsAg

positive subjects may also be HBeAg positive. Although the HBsAg carrier who has anti-HBe cannot be considered non-infectious, the possibility of infection from such patients is much lower than in those without this antibody.

Other hepatitis viruses

13 Hepatitis may also be due to a number of other viruses including hepatitis A virus (HAV). This is a picornavirus which usually causes a milder disease than hepatitis B virus (HBV), is transmitted mainly by the faecal-oral route and chronic infection or virus carriage are not seen.

14 There are probably at least two other hepatitis viruses but although they can be differentiated by exclusion from HAV and HBV there are as yet no specific laboratory tests for their presence. They are therefore referred to as hepatitis non-A and non-B viruses. They can cause severe and recurrent disease and as with HBV a carrier state is recognised.

15 Data are inadequate, but there is no evidence that infection is particularly frequent in those handling routine samples. Hepatitis may occasionally be caused by a number of other viruses, e.g. cytomegalovirus, Epstein-Barr virus and herpes simplex virus.

Conclusions

16 We have concluded that hepatitis B virus should be classified as a group 3 pathogen (see para 21). We recognise that the transmission of hepatitis B by aerosols emanating from blood or serum during common laboratory manipulations is unlikely, but this will not apply to all fluids. We would expect full containment level 3 methods to be used if concentrated or purified virus was being handled. We understand that the procedures required for the safe handling of blood, serum and other samples containing hepatitis B virus are under review and until such time as that review is completed and any new recommendations have been accepted reference must be made to the *Code of Practice for the Prevention of Infection in Clinical Laboratories and Post-mortem Rooms.**

References

- ¹ Zuckerman, A J and Howard, C R *Hepatitis Viruses of Man*. Academic Press, London. 1979.
- ² Alter, H J, Purcell, R H, Gerin, J L, *et al.* 'Transmission of hepatitis B to chimpanzees by hepatitis B surface antigen—positive saliva and semen'. *Infection and Immunity*. Jun. 1977, vol: 16, no. 3, 928–933.
- ³ Bancroft W H, Snitbahn, R, Scott, R M, *et al.* 'Transmission of hepatitis B virus to gibbons by exposure to human saliva containing hepatitis B surface antigen'. *Journal of Infectious Diseases*. Jan. 1977, vol: 135, no. 1, 79–85.
- ⁴ Lauer, J L, Van Drunen, N A, Washburn, J W and Balfour, H H. 'Transmission of hepatitis B virus in clinical laboratory areas'. *Journal of Infectious Diseases*. Oct. 1979, vol: 140, no. 4, 513–516.
- ⁵ Scott, R M, Snitbahn, R, Bancroft, W H, Alter, H J and Tingpalapang, M. 'Experimental transmission of hepatitis B virus by semen and saliva'. *Journal of Infectious Diseases*. Jul. 1980. vol: 142, no. 1, 67–71.
- ⁶ Petersen, N J. 'An assessment of the airborne route in hepatitis B transmission'. *Annals of the New York Academy*. 1980. vol: 353, 157–166.
- ⁷ Petersen, N J, Bond, W W and Favero, M S. 'Air sampling for hepatitis B surface antigen in a dental operator'. *Journal of the American Dental Association* Sept. 1979, vol: 99, no. 3, 465–467.
- ⁸ 'A report by a working party set up by the Medical Research Council Sub-Committee on hepatitis prevention in renal and associated units. Experimental studies on environmental contamination with infected blood during haemodialysis'. *Journal of Hygiene*, Feb. 1975, vol: 74, no. 1, 133–148.

- ⁹ Grist, N R. 'Hepatitis in clinical laboratories'. 1977-78. *Journal of Clinical Pathology*. May 1980, vol: 33, no. 5, 471-473.
- ¹⁰ Grist, N R. 'Hepatitis infection in clinical laboratory staff'. *Medical Laboratory Sciences*. Mar. 1981, vol: 38, no. 2, 103-109.
- ¹¹ Harrington, J M and Shannon, H S. 'Incidence of tuberculosis, hepatitis, and shigellosis in British medical laboratory workers'. *British Medical Journal*. 27 Mar. 1976, vol: 1, no. 6012, 759-762.
- ¹² Polakoff, S. 'Communicable Disease Report'. 1979, Week 48, and 1982, Week 14.
- ¹³ Polakoff, S, Cossart, Y E and Tillet, H E. 'Hepatitis in dialysis units in the United Kingdom'. *British Medical Journal* 8 Jul. 1972, vol: 3, no. 5818, 94-98.
- ¹⁴ Bone, J M, Tonkin, R W, Davidson, A M, Marmion, B P, and Robson, J S. 'Outbreak of dialysis-associated hepatitis in Edinburgh, 1969-70. In *Proceedings of the European Dialysis and Renal Transplantation Association Meeting, Berlin, July 1971*'. 1972, 8, 189-193.
- ¹⁵ Marmion, B P, Burrell, C J and Tonkin, R W. 'High mortality hepatitis B: the Edinburgh outbreak revisited. In *Proceedings of the Third International Symposium on Viral Hepatitis, New York, 1981*'. In preparation.
- ¹⁶ Miyakawa, Y. and Mayumi, M. 'Characterisation and clinical significance of HBeAg. *Proceedings of the Second Symposium on Viral Hepatitis*'. Eds. Vyas, G N, Cohen, S N and Schmid, R. The Franklin Institute Press, Philadelphia, p 193-201.
- ¹⁷ Barbara, J A J. *Personal Communication*.
- ¹⁸ Dow, B C, Macvarish, I, Barr, A, Crawford, R J and Mitchell, R. 'Significance of tests for HEeAg and anti-HBe in HBsAg positive blood donors'. *Journal of Clinical Pathology*. Nov. 1980, vol: 33, no. 11, 1106-1109.

Table 1 Hepatitis B infection in laboratory staff*

<i>Years</i>	<i>Number of cases</i>	<i>Annual average</i>	<i>Estimated number at risk (person-years)</i>	<i>Attack rate</i> [†]
1970–72	17	5.66	36 893	46
1973–74	14	7.0	22 243	63
1975–76	3	1.5	23 142	13
1977–78	6	3.0	27 175	22
1979	0	0.0	11 974	0

* Figures from Grist 1980, 1981.

[†] Per 100 000 person-years.**Table 1A** Hepatitis infections in British clinical laboratories 1980–81.**Hepatitis cases**

<i>Type</i>	<i>Year</i>	<i>Occupation</i>	<i>Comments</i>
A	1981	MLSO, biochemistry	
A	1981	MLSO, haematology	
B	1980	Medical, morbid anatomy	Infected by spouse (carrier)
B*	1980	Medical, morbid anatomy	Laboratory accident
B*	1980	MLSO, haematology	
B*	1981	Phlebotomist	Works in hospital for mentally subnormal
B	1981	MLSO, biochemistry	
? (not B)	1981	Medical, haematology	Silent infection detected by routine screening; laboratory accident
Epstein-Barr virus	1981	MLSO, biochemistry	? Infected by patient contact

From N R Grist J Clin Pathol 1983 36 121–126

* Clinical 'attributable' hepatitis B attack rate = 16/100 000 MLSO Haematology.
 83/100 000 Medical Morbid Anatomy.
 50/100 000 Phlebotomists.
 9/100 000 Total Staff.

Table 2 Hepatitis B infection in laboratory staff in England and Wales and Northern Ireland

<i>Epidemiological year weeks 27–26 incl.</i>	<i>CDR reports of acute hepatitis B</i>	
	<i>Number of laboratory staff*</i>	<i>Total number</i> [†]
1972–	8	681
1973–	9	779
1974–	7	913
1975–	3	1 061
1976–	3	1 067
1977–	4	1 223
1978–	3	980
1979–80	2	1 000

Data from Polakoff, Communicable Disease Report 79/48.

* Includes all categories working in laboratory—medical, scientific, technical and ancillary.

[†] This is probably an underestimate. In many cases, especially those that are clinically mild, specimens are not submitted for the appropriate laboratory tests.

Table 2A Hepatitis B infection in health service staff in England

<i>Health service staff category</i>	<i>Mid-period number</i>	<i>Acute hepatitis B incidence CDR years 1975-79</i>	
		<i>CDR acute HB 1975-79</i>	<i>Average annual rate per 100 000</i>
Surgeons	10 372	10	19
Physicians	43 828	39	18
Medical laboratory	2 232	4	36
Laboratory (scientific and technical)	14 291	13	18
Nursing staff	391 953	136	7
Dentists	14 354	12	17
Staff MSN institutions *	28 000	43	31

Data from Polakoff, Communicable Disease Report 82/14.

* Approximate number, supplied by the DHSS, of all staff with patient contact in England and Wales: the number of cases and the rate for this group are for England and Wales together.

Table 3 Hepatitis B infection in laboratory staff in England, Wales, Northern Ireland and Scotland

<i>Epidemiological year</i>	<i>Number of cases</i>
1975-	3
1976-	3
1977-	5
1978-	4
1979-80	3

Figures from Communicable Disease Report 79/48 (as in Table 2) with additional Scottish data from records of Communicable Diseases Scotland Unit.

Table 4 Outbreaks of hepatitis B in dialysis units: staff affected

<i>Outbreaks</i>	<i>Dates</i>	<i>Numbers of staff</i>	<i>Deaths</i>
Manchester	1965-66	11	3*
Edinburgh	1969-71	8	4*
Liverpool	1966-71	33	0
Birmingham	1967-71	12	0
Royal Free	1969-70	8	0
Guys	1969-71	42	0
Cardiff	1969-71	4	0

* Three of the seven deaths were in technical staff.
We are indebted to Dr J V S Pether for providing data.

Appendix I

Training of laboratory personnel in microbiological safety

- 1 Safety training is an important factor in achieving high standards in health and safety at work and the general principles of occupational hygiene and safety should be included in the syllabus of all professional bodies and teaching establishments concerned with the professional training of medical, veterinary, scientific and technical students.
- 2 Employers have a responsibility under the HSW Act for training their personnel in matters specific to the workplace. This training should include instruction in the nature of the potential hazards and in the practical use of special procedures, techniques and safety equipment that are required to minimise the risks. Employees also have a duty to comply with the safety measures which are provided for their protection.
- 3 The employer, or the employing body, should appoint a person for the management of health and safety training. This could form part of the duties of the safety officer who should regularly review the standards required in consultation with the safety committee.* New members of staff should not be permitted to work with pathogens or infective materials until they have undergone a comprehensive training course with practical training in the procedures and manipulations appropriate to the work. The course, suitably modified in content, should be extended to all grades of laboratory personnel.
- 4 Auxiliary and cleaning staff must also receive instruction in the local health and safety procedures and must fully understand the instructions. This will be particularly important where the management of the laboratory is not primarily responsible for the recruitment and supervision of such staff.
- 5 Refresher courses and lectures will be necessary to keep personnel up to date with changes in equipment, materials and techniques. A wide variety of audio visual aids are also available and some colleges and health authorities offer courses on microbiological safety.

* Safety Committees and Safety Representatives Regulations 1977.

Appendix J

Pathogens controlled by the Agriculture and Fisheries Departments

Pathogens of animals and poultry

1 The Importation of Animal Pathogens Order 1980 defines 'animals' as cattle, sheep, goats, all other ruminating animals, horses and swine. The Order prohibits the importation into Great Britain of any animal pathogen or carrier except under the authority of a licence in writing issued by the appropriate Minister and in accordance with the conditions of that licence. The 'appropriate Minister' in the application of this Order to England means the Minister of Agriculture, Fisheries and Food, in the application of this Order to Scotland means the Secretary of State for Scotland, and in the application of this Order to Wales means the Secretary of State for Wales.

2 The pathogens of most concern to the Agriculture Departments are listed below and those shown in capital letters cause diseases which are notifiable and subject to statutory control by Orders made under the Animal Health Act 1981. The Act provides for the control of certain diseases of animals as defined above and also of poultry, which are defined in the Act as domestic fowls, turkeys, geese, ducks, guinea-fowls, pigeons, pheasants and partridges.

Bacteria and Mycoplasmas

Arizona spp
BACILLUS ANTHRACIS
BRUCELLA spp (abortus, suis and melitensis)
CHLAMYDIA PSITTACI
Francisella tularensis
MYCOBACTERIUM spp
Mycoplasma agalactiae
MYCOPLASMA MYCOIDES
Mycoplasma mycoides subsp. *capri*
PSEUDOMONAS MALLEI
SALMONELLA spp
Yersinia pestis

Viruses

Bunyaviridae

Akabane virus
Nairobi sheep disease and Ganjam viruses (Nairoviruses)
Rift Valley fever virus (Phlebovirus)

Caliciviridae

Vesicular exanthema virus (Calicivirus)

Herpesviridae

AUJESZKY'S DISEASE VIRUS (Suid herpesvirus 1, Pseudorabies)
Duck enteritis virus (Duck plague virus)
Equine rhinopneumonitis viruses (Equid herpesviruses)
Malignant catarrhal fever virus

Iridoviridae

AFRICAN SWINE FEVER VIRUS

Orthomyxoviridae

AVIAN INFLUENZA VIRUS (HAV 1-8) (Influenzavirus, Fowl plague)
Equine influenza viruses (Influenzavirus)
Swine Influenza viruses (Influenzavirus)

Paramyxoviridae

NEWCASTLE DISEASE VIRUS (Paramyxovirus)
RINDERPEST AND PESTE DES PETITS RUMINANTS VIRUSES
(Morbilliviruses)

Picornaviridae

FOOT-AND-MOUTH DISEASE VIRUS (Aphthovirus)
SWINE VESICULAR DISEASE VIRUS (Enterovirus)
TESCHEN DISEASE VIRUS (Enterovirus)

Poxviridae

Camelpox virus (Orthopoxvirus)
Goat pox virus (Capripoxvirus)
Horse pox virus;
Lumpy Skin Disease virus (Capripoxvirus)
Sheep pox virus (Capripoxvirus)

Reoviridae

AFRICAN HORSE SICKNESS VIRUS (Orbivirus)
Bluetongue virus (Orbivirus)
Epizootic haemorrhagic disease of deer virus (Orbivirus)
Ibaraki virus (Orbivirus)

Retroviridae

ENZOOTIC BOVINE LEUKOSIS VIRUS (Oncovirus)
EQUINE INFECTIOUS ANAEMIA VIRUS
Maedi/Visna virus (Lentivirus)

Rhabdoviridae

Ephemeral fever virus
RABIES VIRUS (Lyssavirus)
Vesicular stomatitis virus (Vesiculovirus)

Togaviridae

EQUINE ENCEPHALOMYELITIS VIRUSES (Eastern and Western)
(Alphaviruses)
Equine arteritis virus
SWINE FEVER VIRUS (Pestivirus)
VENEZUELAN EQUINE ENCEPHALOMYELITIS VIRUS (Alphavirus)
Wesselsbron virus (Flavivirus)

Parasites

Anaplasma spp
Theileria spp

TRYPANOSOMA EQUIPERDUM

Other trypanosoma species

3 Details of the requirements for the importation or handling of pathogens of animals or poultry may be obtained from:

Ministry of Agriculture, Fisheries and Food
Animal Health Division
Government Buildings
Hook Rise South
Tolworth
Surbiton
Surrey KT6 7NF (Tel: 01-337-6611)

Department of Agriculture and Fisheries for Scotland
Chesser House
500 Gorgie Street
Edinburgh EH11 3AW (Tel: 031-443-4020)

Welsh Office, Agriculture Department
Crown Buildings
Cathays Park
Cardiff (Tel: 0220-825111)

Pathogens of other animals

4 The following virus of rabbits is controlled by an Order made under the Pests Act 1954.

Poxviridae

Myxoma virus (Leporipoxvirus).

5 Details of the requirements may be obtained from:

Ministry of Agriculture, Fisheries and Food
Worplesdon Laboratory
Tangley Place
Worplesdon
Surrey GU8 3LQ (Tel: 0483-232581)

Pathogens of plants

6 The Import/Export (Plant Health) (Great Britain) Order 1980 and the Plant Pests (Great Britain) Order 1980, made under the Plant Health Act 1967, prohibit the importation into Great Britain and the keeping of any non-indigenous plant pathogen or plant pest, except under the authority of a licence in writing issued by the appropriate Minister and in accordance with the conditions of that licence. The Plant Pests Order also requires that the appropriate Minister is notified in writing of the presence or suspected presence of any non-indigenous plant pathogens or plant pest.

7 The following pathogens and pests are controlled by specific Orders made under the Act;

Bacteria

Erwinia amylovora
Erwinia salicis

Fungi

Ceratocystis ulmi
Phytophthora fragariae
Synchytrium endobioticum
Verticillium albo-atrum

Parasites

Cacoeccimorpha pronubana
Epichoristodes acebella
Globodera pallida
Globodera rostochiensis
Leptinotarsa decemlineata
Heterodera schachtii

Viruses

Plum pox virus

8 Details of the requirements of the various Orders and for the importation and handling of plant pathogens may be obtained from:

Ministry of Agriculture, Fisheries and Food
Harpenden Laboratory
Hatching Green
Harpenden
Herts AL5 2BD (Telephone 05827–5241)

or

Department of Agriculture and Fisheries for Scotland
Agricultural Science Services
East Craigs
Edinburgh EH12 8NJ

Pathogens of fish

9 The following pathogens of fish cause diseases which are currently notifiable and controlled by Orders made under the Diseases of Fish Act, 1937. (Note: there is the possibility of changes in legislation which will remove some of these from the notifiable diseases list and add others).

Bacteria

Aeromonas salmonicida
Flexibacter columnaris
Renibacterium salmoninarum

Parasites

Myxosoma cerebralis

Viruses

Birnaviridae

Infectious pancreatic necrosis virus

Rhabdoviridae

Viral haemorrhagic septicaemia virus
Infectious haematopoietic necrosis virus
Spring viraemia of carp virus (*Rhabdovirus carpio*)

10 Details of the requirements may be obtained from:

Ministry of Agriculture, Fisheries and Food
Fish Disease Laboratory
The Nothe
Weymouth
Dorset DT4 8UB (Tel: 03057-72137)

References

- 1 Report of the Committee of Inquiry into the smallpox outbreak in London in March and April 1973, (Cmnd 5626), HMSO, 1974. 164pp. ISBN 0 10 156260 8.
- 2 Report of the working party on the laboratory use of dangerous pathogens, (Cmnd 6054), HMSO, 1975. 44pp. ISBN 0 10 160540 4.
- 3 Control of laboratory use of pathogens very dangerous to humans, DHSS *et al*, 1976.
- 4 Code of Practice for the Prevention of Infection in Clinical Laboratories and Post-mortem Rooms, DHSS *and others*, HMSO, 1978. 75pp. ISBN 0 11 320464 7.
- 5 Report of the investigation into the cause of the 1978 Birmingham smallpox occurrence, HMSO, 1980. 216pp. ISBN 0 10 26680 9.
- 6 Report of the Robens Committee on safety and health at work, (Cmnd 5034), HMSO, 1972. 218pp. ISBN 0 10 150340 7.
- 7 Bergey's Manual of Determinative Bacteriology 8th Ed. Baltimore: Williams and Wilkins 1974. 1268pp. ISBN 0 683 01117 0.
- 8 Approved Lists of Bacterial Names. Skerman *and others*, Intl J Syst Bact, 1980, vol: 30, 225–420.
- 9 Approved Names of Biomedically Important Bacteria: WHO Terminology Circular TXB–1 (TER/81.1, November 1981), WHO Geneva.
- 10 British Society for Mycopathology Nomenclature of fungi pathogenic to man and animals MRC Memorandum 23 4Ed (1977) HMSO, London.
- 11 Fourth Report of the International Committee on Taxonomy of Viruses (1982) Matthews R E F, Basel S Karger. 200pp. ISBN 3 8055 3557 0.
- 12 Parasitology: The biology of animal parasites, 5th edition (1982). Elmer R Noble and Glenn A Noble. Lea and Febigier, Philadelphia. 522pp. ISBN 0 8121 8819 1.

Other reading

Redgrave's Health and Safety in Factories 2nd ed. 1982, Butterworth & Shaw, London. 1932pp. ISBN 0 406 35307 7.

Bacterial and Viral Zoonoses. Report of a WHO Expert Committee with the Participation of FAO. Technical Report Series 682, WHO Geneva 1982. ISBN 92 4 120682 9.

Laboratory Acquired Infections. History Incidence, Causes and Prevention. C H Collins, Butterworth, London 1983. 277pp. ISBN 0 408 10650 6.

Laboratory Biosafety Manual. WHO, Geneva 1983. 123pp. ISBN 92 4 1541679.